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Proposed Re-evaluation Decision

Nicosulfuron

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Overview

Proposed Re-evaluation Decision for Nicosulfuron

After a re-evaluation of the herbicide nicosulfuron, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing nicosulfuron in Canada.

An evaluation of available scientific information found that products containing nicosulfuron have value in the food and crop industry and do not present unacceptable risks to human health or the environment. As a condition of the continued registration of nicosulfuron use on field corn, sweet corn and lowbush blueberries, new risk reduction measures are proposed for inclusion on the labels of all products. No additional data are being requested at this time.

The PMRA's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the detail of the re-evaluation activities and program structure. Re-evaluation draws on data from registrants, published scientific reports, information from other regulatory agencies and any other relevant information available.

This proposal affects all end-use products containing nicosulfuron registered in Canada. Once the final re-evaluation decision is made, registrants will be instructed on how to address the new risk-reduction measures.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for nicosulfuron and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessment of nicosulfuron.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*

What Does Health Canada Consider When Making a Re-evaluation Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration[2]. The Act also requires that products have value[3] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies rigorous, modern hazard and risk assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in both humans (e.g. children) and organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

Before making a re-evaluation decision on nicosulfuron, the PMRA will consider all comments received from the public in response to this consultation document[4]. The PMRA will then publish a Re-evaluation Decision document[5] on nicosulfuron, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

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2 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*

3 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

4 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*

5 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*

What is Nicosulfuron?

Nicosulfuron is a selective systemic sulfonylurea herbicide. It is registered for postemergent use on terrestrial food and feed crops including field corn, sweet corn, seed corn (inbred lines grown in Eastern Canada only) and lowbush blueberries (Eastern Canada only). It may be used alone to control quackgrass and annual grassy weeds or in co-formulation with rimsulfuron to control quackgrass and annual grassy weeds as well as redroot pigweed (including triazine resistant varieties) and black bulrush. Nicosulfuron is to be applied once per year at a rate of 12.5–25 g a.i./ha by ground equipment only.

Health Considerations

Can Approved Uses of Nicosulfuron Affect Human Health?

Nicosulfuron is unlikely to affect your health when used according to label directions.

People could be exposed to nicosulfuron by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the dose levels where no health effects occur and the dose levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when using nicosulfuron products according to label directions.

An acute overexposure to very high doses of nicosulfuron can produce a variety of symptoms in animals and humans. Symptoms may include a decrease in motor activity and weight loss. Local effects of an acute dermal exposure may include erythema, edema, and skin sensitization. Contact with the eye may cause corneal opacity, conjunctival redness, iritis and chemosis. To prevent overexposure, label directions must be followed.

Additional toxic effects on the liver, ovaries, pancreas and kidney, as well as effects noted in pregnant females (increased abortions and mortality), were observed in animals at very high, multiple doses and would not likely occur when nicosulfuron products are used according to label directions. Based on the weight of evidence, nicosulfuron is considered non-carcinogenic, therefore, a cancer risk assessment was not required.

Although there are no risks of concern based on current uses of nicosulfuron, some additional protective measures have been proposed for inclusion on product labels to update the label according to current standards.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Human exposure to nicosulfuron was estimated from residues in treated crops and drinking water, including the most highly exposed subpopulation (e.g. children 1 to 6 years old). This aggregate exposure (i.e. to nicosulfuron from food and drinking water) represents less than 1% of the chronic reference dose.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for the *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

MRLs for nicosulfuron are currently specified for blueberries and corn or processed foods derived from these foods. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. The proposed MRL amendments for nicosulfuron can be found in the Science Evaluation Section 8.1.2 of this consultation document.

Risks in Residential and Other Non-Occupational Environments

Residential and other non-occupational risks are not of concern.

Nicosulfuron is not registered for use in any residential areas; therefore, no residential or other non-occupational risks are expected.

Occupational Risks From Handling Nicosulfuron

Occupational risks are not of concern.

Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation, and with the use of appropriate protective equipment, the risk estimates associated with mixing, loading and applying activities meet current standards for all the scenarios and are not of concern. The proposed personal protection equipment are long pants, long-sleeved shirt, socks, chemical-resistant gloves and footwear.

Occupational postapplication risks are not of concern.

Occupational postapplication risk assessments consider exposures to workers re-entering treated sites. Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation and the proposed protective measures (revised re-entry interval), the postapplication exposure risk estimate for re-entry workers performing high exposure activities (scouting) meet current standards and are not of concern.

Environmental Considerations

What Happens When Nicosulfuron is Introduced Into the Environment?

Nicosulfuron poses a potential risk to terrestrial plants, therefore, additional risk mitigation measures need to be observed.

Nicosulfuron released into the environment may be found in soil and surface water. However, nicosulfuron is broken down by microorganisms and/or by chemical reaction with water, and it is not expected to persist in terrestrial and aquatic environments, except under anaerobic (low oxygen) conditions in soils where it can be persistent. In anaerobic aquatic environments it is not persistent. Several major products from the breakdown of nicosulfuron will be present in soil and aquatic systems, and three of these can persist for longer periods of time than nicosulfuron. Field evidence indicates that nicosulfuron remains within the top 50 cm of the soil after application, and its use will not result in significant groundwater contamination. Water monitoring data indicate that nicosulfuron can occur in runoff. However, the concentrations are very low and do not pose a concern for aquatic life.

The use of nicosulfuron is a potential concern for terrestrial habitats that may contain sensitive plant species. To reduce exposure to plants, it is important that risk reduction measures such as buffer zones are observed. The risk to wild birds, mammals, bees, earthworms, fish, amphibians, aquatic invertebrates, aquatic plants and algae from nicosulfuron was not found to be a concern. The major breakdown products of nicosulfuron were not found to be a concern to terrestrial and aquatic life.

Value Considerations

What is the Value of Nicosulfuron?

Nicosulfuron controls quackgrass and many annual grassy weeds in corn at a low application rate.

Nicosulfuron reduces a portion of the economic losses caused by weeds, estimated at $59.8 million in the early 1990s for field corn, sweet corn and blueberry. Nicosulfuron (co-formulated with rimsulfuron) is the only herbicide registered for the control of black bulrush in lowbush blueberries. Compared to alternative non-sulfonylurea postemergent grass herbicides, nicosulfuron has greater flexibility in application timing and is applied at a low rate which lessens the chemical load in the environment. Although nicosulfuron plays a role in mitigating resistance development in weeds to other herbicide groups, resistance management must be considered as more weed species are reported to be resistant to herbicides that inhibit acetolactate synthase (such as nicosulfuron) than to herbicides having other modes of action.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of nicosulfuron, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- To protect mixer/loader/applicators: additional protective equipment
- To protect workers re-entering treated sites: a restricted-entry interval
- To protect workers using wettable granular formulation: additional precautionary statements and directions for use
- To avoid drift to areas of human habitation or areas of human activity: precautionary statements

Environment

- To protect sensitive terrestrial plant species: additional precautionary statements and directions for use, as well as buffer zones to protect non-target terrestrial plants from spray drift.

- To protect aquatic plants and algae: additional precautionary statements including statements for sites with characteristics that may enhance runoff when heavy rain is forecast.

Next Steps

Before making a re-evaluation decision on nicosulfuron, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision document, which will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

Other Information

When the re-evaluation decision is made, the PMRA will publish an Evaluation Report on nicosulfuron in the context of this re-evaluation decision (based on the Science Evaluation section of this consultation document). In addition, the test data on which the decision is based will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

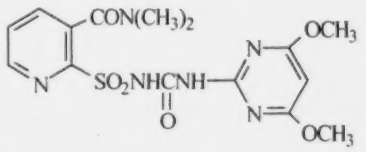
1.0 Introduction

Nicosulfuron is a selective systemic herbicide. It belongs to the sulfonylurea chemical family and is classified as a Group 2 herbicide. The herbicidal activity of nicosulfuron is due to the inhibition of the plant enzyme acetolactate synthase (ALS), also called acetohydroxyacid synthase (AHAS).

Following the re-evaluation announcement for nicosulfuron, E.I. du Pont Canada Company, the registrant of the technical grade active ingredient (TGAI) and primary data provider in Canada, indicated it would continue to support all uses included on the label of Commercial Class end-use products. There are no Domestic Class products containing nicosulfuron registered in Canada.

2.0 The Technical Grade Active Ingredient, its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Nicosulfuron
Function	Herbicide
Chemical family	Sulfonylurea
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	2-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-*N*,*N*-dimethylnicotinamide
2. Chemical Abstracts Service (CAS)	2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-*N*,*N*-dimethyl-3-pyridinecarboxamide
CAS Registry Number	111991-09-4
Molecular formula	$C_{15}H_{18}N_6O_6S$
Molecular weight	410.4
Structural formula	

Purity:	93% NS (limits: 90.21–95.79 %)
Basic Manufacturer:	Dupont Agricultural Caribe Industries, Ltd. Manati, Puerto Rico

Identity of relevant impurities of toxicological, environmental and/or other significance:

Based on the manufacturing process, the product is not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, Appendix II.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	1.6×10^{-14} Pa
Ultraviolet–visible spectrum	not expected to absorb UV at $\lambda > 300$ nm
Solubility in water at 20°C	pH — w % (g/100g) 5 — 0.04 7 — 1.2 9 — 3.92
n-Octanol–water partition coefficient (K_{ow})	pH — Log K_{ow} 5 — −0.36 7 — −1.8 9 — −2.0
Dissociation constant (pK_a)	p*K*a = 4.3

2.3 Description of Registered Nicosulfuron Uses

Appendix I lists all nicosulfuron products registered under the authority of the *Pest Control Products Act*, specifically including one technical grade active ingredient, two manufacturing concentrates and three Commercial Class end-use products. One Commercial Class end-use product contains nicosulfuron alone while the remaining two nicosulfuron products are co-formulated with rimsulfuron.

Appendix II lists all the uses for which nicosulfuron is presently registered. All uses were supported by the registrant at the start of the re-evaluation and were, therefore, considered in the health and environmental risk assessments. Also presented is whether any of the uses were added through the PMRA minor use program. While currently supported by the registrant, the data supporting these minor uses were originally generated by a user group.

Uses of nicosulfuron belong to the following use site categories: terrestrial food crops and terrestrial feed crops. The crops specifically include corn (field, sweet, and seed corn inbreds) and lowbush blueberry.

3.0 Impact on Human and Animal Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels where no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to the effects of a chemical than the most sensitive animal species. The health effects noted here were observed in animals at dose levels at least 100-fold (often much higher) above levels to which humans are normally exposed through use of products containing this chemical.

3.1 Toxicological Summary

The toxicology database supporting nicosulfuron is primarily based on studies from the technical registrant. In laboratory animals, nicosulfuron is of low acute toxicity by the oral, dermal, and inhalation routes of exposure, non-irritating to rabbit skin, moderately irritating to rabbit eyes, and a skin sensitizer in Guinea pigs. Signs of acute toxicity induced by very high doses of nicosulfuron are weight loss and reduced motor activity.

With oral exposure, nicosulfuron is rapidly absorbed from the gastrointestinal tract with peak blood levels occurring within one hour. Accumulation within tissues is minimal. Excretion is rapid, with the largest amount occurring in the feces (e.g. 81–88% in feces with a 20.1–26.2% biliary component; 13–20% in the urine). The majority of the radioactive nicosulfuron was excreted as the parent compound. A minor amount may be hydroxylated at the 5′ carbon on the pyrimidine portion of the molecule before or following hydrolytic cleavage of the pyrimidine and pyridine portions. A number of minor metabolites were found in both urine and feces.

In short- and long-term studies, the major effect was a reduction in body weight or body-weight gain. In subchronic mouse, rat and dog studies, reduced body-weight gains occurred with a reduction in food consumption. In the dog studies, liver weights increased along with an increase in enzyme activity indicative of hepatotoxicity (e.g. alanine aminotransferase, alkaline phosphatase).

In a chronic study in the mouse, body weight was reduced with a slight increase (relative and absolute) in liver weight. There was a treatment-related increase in the number of hepatocellular tumours (liver masses, adenomas, carcinomas) in the male mouse, however this increase was seen only at a very high dose level (>6000 mg/kg bw/day) which was greatly in excess of the recommended limit dose of 1000 mg/kg bw/day. In a chronic rat study there was a decrease in body-weight gain in addition to a number of miscellaneous effects at the highest dose (>2000 mg/kg bw/day) only. All genotoxicity studies were negative. Nicosulfuron is considered non-carcinogenic.

In a rat reproduction study and a rabbit developmental study, reductions in body-weight gain and food consumption were also noted. Reproductive and offspring sensitivities were not observed.

Reference doses have been set based on the NOAEL for the most sensitive indicator of toxicity, namely body weight and organ (liver, kidney) weight effects in dogs. Reference doses incorporate uncertainty factors to account for extrapolating between laboratory animals and humans.

The toxicology profile and toxicology endpoints used in the risk assessment of nicosulfuron are summarized in Appendix III and IV.

3.2 Occupational and Non-occupational Risk Assessment

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant NOAEL from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE which incorporates safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean exposure will result in adverse effects. However, MOEs less than the target MOE require measures to reduce risk.

3.2.1 Toxicological Endpoints

To estimate risk for short-, intermediate- and long-term oral, dermal and inhalation exposure, an oral NOAEL of 141.1 mg/kg bw/day from a one-year dog study was used. The NOAEL was based on decreased body weight and body-weight gain, and increased relative liver and kidney weights in the male at the LOAEL of 571 mg/kg bw/day. A target **MOE of 100** is based on the standard uncertainty factors of 10 for interspecies extrapolation, 10 for intraspecies variability.

Based on weight-of-evidence, the PMRA does not consider nicosulfuron to be a possible human carcinogen.

Dermal Absorption
The PMRA can estimate dermal absorption by considering physical and chemical properties of a substance (e.g. molecular weight, log K_{ow} and solubility) and/or by considering chemical-specific dermal absorption data (e.g. in vivo rat dermal absorption study). Based on a first tier risk

assessment, a default dermal absorption factor of 100% was used. No chemical specific dermal absorption data were available for the estimation of dermal absorption.

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to nicosulfuron through mixing, loading and/or applying the pesticide, and when re-entering a treated site to conduct activities such as scouting and/or handling of treated crops.

Mixer/Loader/Applicator Exposure and Risk Assessment
There are potential exposures to mixers, loaders, applicators and other handlers. The following major exposure scenarios were assessed:

- Mixing and loading wettable granules in water-soluble package (WSP).
- Mixing, loading and applying wettable granules in WSP by low pressure handwand and backpack.
- Applying by groundboom sprayer.

Occupational handlers of nicosulfuron include farmers and custom agricultural applicators who mix, load and apply the herbicide. One application is permitted per season and based on the timing of application and use pattern, the duration of exposure for farmers and custom applicators is expected to be short- (1–30 days) or intermediate-term (1–6 months).

Exposure for all crop scenarios is predominantly dermal, with inhalation accounting for a minor component of overall exposure. The toxicological endpoint for these scenarios is based on an oral NOAEL from a one-year dog study. Because no dermal absorption study was available, the PMRA will use a dermal absorption factor of 100% as a part of a first tier exposure risk assessment.

The PMRA estimated handler exposure based on the following level of personal protective equipment (PPE) :

Baseline PPE : Long pants, long-sleeved shirt and chemical-resistant gloves (gloves not required for groundboom sprayers).

Mixer/loader/applicator exposure estimates are based on the best available data at this time. The assessment might be refined with product-specific exposure data, biological monitoring data, and/or dermal absorption data.

No chemical specific exposure studies were available for use in the re-evaluation of nicosulfiron. Thus, appropriate dermal and inhalation exposures were estimated using the *Pesticide Handlers Exposure Database (PHED), Version 1.1*. PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment.

In some cases, PHED did not contain appropriate data sets to estimate exposure to workers wearing additional PPE and/or using engineering controls. Surrogate data for wettable granules in WSP were not available in PHED, therefore closed mixing and loading data for wettable granules were used.

For some scenarios (e.g. hand-held equipment), estimating exposure from mixing, loading and applying wettable granules in WSP was not possible using PHED. In these situations, exposure units from mix/load/apply with open pour liquid for low pressure handwand and backpack were used.

PHED unit exposures coupled with information on the amount of nicosulfuron handled per day was used to estimate handler exposure. The amount handled per day is based on the maximum label application rate and default assumptions on the area (of crop) that can reasonably be treated in one day.

Calculated MOEs exceed the target MOE for all exposure scenarios and are summarized in Table 1 of Appendix V.

Postapplication Worker Exposure and Risk Assessment

Workers who re-enter treated sites to conduct activities involving foliar contact may be exposed to nicosulfuron. Based on the crops and their associated re-entry activities, exposure to nicosulfuron is expected to be short-term (1 to 30 days) in duration. One application per crop per season is expected (as per product labels) and postapplication exposure may occur from hand detasseling, hand harvesting, hand pruning, hand weeding, irrigation, scouting and thinning.

Default dislodgeable foliar residue (DFR) values and activity specific transfer coefficients (TC) were used to estimate postapplication exposure resulting from contact with treated foliage at various times after application. DFR data represent the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant. In this case, no DFR studies were submitted, therefore, a default peak DFR value of 20% of the application rate with 10% dissipation per day was used. A TC represents the amount of foliar contact per unit time and relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples, scouting late season cotton) and reflect standard agricultural work clothing worn by adult workers. The primary postapplication exposure activity is scouting.

The postapplication risk estimates include a number of conservative inputs, such as the assumption that workers are exposed to residues following the maximum number of applications at the maximum rate.

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely re-enter. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE. Calculated MOEs exceed the target MOE on day 0, and proposed REIs are set at 12 hours. Postapplication exposure calculations for each use site are summarized in Table 2 of Appendix V.

3.2.3 Non-occupational Exposure and Risk Assessment

3.2.3.1 Residential Handler Risk

There are no domestic class products registered in Canada; therefore, a residential handler risk assessment was not required.

3.2.3.2 Bystander Exposure and Risk

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible, thus, a bystander exposure risk assessment was not required.

3.3 Dietary Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to nicosulfuron from treated imports is also included in the assessment. These dietary assessments are age specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when risk exceeds 100% of the reference dose. PMRA's Science Policy Notice SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute and chronic risk assessments procedures.

Residue estimates used in the dietary risk assessment (DRA) may be conservatively based on the maximum residue limits (MRL) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program (PDP).

Chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.03), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendix VI and VII.

3.3.1 Determination of Acute Reference Dose

An acute (1 day) reference dose (ARfD) was not calculated since there was not an acute endpoint of concern.

3.3.2 Determination of Acceptable Daily Intake

The acceptable daily intake (ADI), which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects, was based on a NOAEL of 141.1 mg/kg bw/day from a one-year feeding study in dogs. The endpoint selected was based on decreased body weight and body-weight gain in the male and increased relative liver and kidney weights, also in the male, at a LOAEL of 571 mg/kg bw/day. An overall uncertainty factor of 100 was required to account for interspecies extrapolation (10-fold) and intraspecies variability (10-fold), resulting in an ADI of 1.41 mg/kg bw/day (141.1 mg/kg bw/day ÷ 100). This value was considered protective of all populations, including infants and children, and females of childbearing age (13–49 years).

3.3.3 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is acceptable.

The chronic potential daily intake from all sources (food and drinking water) accounted for less than 1% of the ADI for all subpopulations and is, therefore, not of concern.

3.3.4 Cancer Potency Factor

A cancer risk assessment was not conducted since the nicosulfuron database did not suggest any carcinogenic potential in mice or rats.

3.3.5 Carcinogenic Dietary Exposure and Risk Assessment

A cancer risk assessment was not conducted since the nicosulfuron database did not suggest any carcinogenic potential in mice or rats.

3.4 Exposure From Drinking Water

3.4.1 Concentrations in Drinking Water

Nicosulfuron residues in drinking water sources were estimated using computer simulation models. The chronic estimated drinking water concentration value used in the exposure model is 3.94 ppb.

3.4.2 Drinking Water Exposure and Risk Assessment

Drinking water estimates were incorporated directly in the exposure model. For more information, please refer to the aggregate risk assessment (Section 3.5).

3.5 Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation).

As residential use of nicosulfuron is not permitted, aggregate exposure is from dietary and drinking water exposures only (see Sections 3.3 and 3.4). Chronic aggregate (food and water) exposures were less than the respective reference doses. Therefore, aggregate exposure from all relevant sources is not considered a health concern.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Nicosulfuron is very soluble in water. It is slightly volatile from plant leaves and soil. However, it is not likely to volatilize from water under field conditions owing to its high solubility. Nicosulfuron is unlikely to bioaccumulate or bioconcentrate in organisms. Environmental fate data for nicosulfuron are summarized in Table 1 of Appendix X. Nicosulfuron is a labile chemical and the main route of transformation in soil and aquatic systems is biotransformation. Hydrolysis becomes an important route of transformation under acidic conditions (e.g. pH 5). At cooler temperatures (e.g. 5°C) the transformation of nicosulfuron is slowed considerably. Laboratory and field studies indicate that nicosulfuron is moderately persistent in soil. Applications to soil dissipate within a year. The major transformation products (>10% of applied active) are ADMP, HMUD, AUSN, IN-HYY21, INJ0290, IN-V9367 and IN 37740 (see list of abbreviations in Appendix IX). Some of these (ASDM, AUSN) were more persistent than nicosulfuron in soils. In water/sediment systems the transformation products are largely associated with the aqueous phase. There is evidence that nicosulfuron can be persistent in anaerobic (flooded) soils. However, in anaerobic aquatic systems nicosulfuron transforms at about the same rate as aerobic systems.

Soil column leaching studies indicate that nicosulfuron is highly mobile in a variety of soils. Adsorption properties of the major transformation products indicate they are also potentially highly mobile in soils. However, soil lysimeter studies conducted in the field indicate that nicosulfuron leaching is limited to a depth of 50 cm. The discrepancy between the column leaching and the field studies is attributed to biotransformation as nicosulfuron moves downward through the soil profile. In addition, it may also be due to the gradual incorporation of nicosulfuron into soil mineral lattices in the lysimeter studies, thereby rendering it immobile. This may be related to the slower rate of leaching observed in the field.

As indicated in Appendix IV, nicosulfuron is not included as an analyte in surface water or groundwater monitoring data collected by Canadian federal, provincial and territorial government departments, or by the United States Geological Survey or the Environmental Protection Agency. A single study of sulfonylurea herbicides in several small water basins in North Dakota found nicosulfuron to be the most frequently detected herbicide in the sulfonylurea class (about 30% of samples collected). However, the concentrations detected were low (maximum 0.06 µg/L).

4.2 Effects on Non-target Species

The environmental risk assessment determines the potential for adverse ecological effects in each environmental compartment by comparing the ratio of the estimated environmental exposure to the ecotoxicological effect. The estimated environmental exposure concentration (EEC) is the initial or cumulative concentration of pesticide in the various sources of food, water and soil to which the organism is exposed. EECs are calculated by different methods for each media (food, water or soil). If multiple applications of pesticide are used, cumulative EECs are determined by using the time taken to decline to 50% of the original application (DT_{50}) using the minimum time interval between applications for each environmental media.

The risk assessment is initially conducted using a screening-level scenario which assumes maximum exposure (EEC) and the most sensitive toxicological endpoint for the organism of interest. This assumes direct application or overspray to the environmental media (food, water, soil) to which the organism is exposed. This is the most conservative scenario and generally does not reflect the exposure to which an organism would be subject to when the pesticide is applied according to the label instructions. Risk to the environment is calculated as a risk quotient (RQ) which is the ratio between the environmental exposure and the toxicological endpoint for the organism (i.e. RQ = EEC/toxicological endpoint). The threshold or level of concern for potentially harmful effects to an organism is an RQ value of 1 where the exposure exactly equals the toxicological endpoint. RQ values greater than or equal to 1 are considered to equal or exceed the level of concern which may result in potentially harmful effects to the organism. RQ values less than 1 indicate negligible risk to the organism because they are below the threshold for harmful effects. In the latter case, no further assessment is carried out. If the RQ is greater than or equal to 1, the level of concern, then a refinement of the risk assessment is carried out to assess the level of concern using scenarios which are a better approximation of exposure or toxicological effects and less conservative. Refinements can include (i) exposure from the fraction of pesticide which drifts onto non-target habitats, instead of assuming 100% overspray, and (ii) exposure from the amount of pesticide predicted in runoff, instead of assuming direct

overspray to water (i.e. 100% exposure). The refinements may also consider different toxicity endpoints or a percentile of a species sensitivity distribution rather than the most sensitive endpoint. They may also consider the results of a mesocosm study using several species rather than the toxicity from a single species. Further refinements to the risk assessment may consider the use of monitoring data collected in the field rather than EECs generated by a model.

4.2.1 Effects on Terrestrial Organisms

The assessment of the toxicity of nicosulfuron to terrestrial organisms involved an evaluation of most sensitive endpoints for the earthworm (acute contact), the honey bee (acute contact), three species of birds (acute oral, dietary, and reproductive toxicity), two species of mammals (acute oral, dietary, and reproductive toxicity), and 22 species of terrestrial plants (seed germination, seedling emergence and vegetative vigour). The terrestrial toxicity data for nicosulfuron are summarized in Table 2 (Appendix X). The toxicity endpoints used in the screening level risk assessment were the most sensitive (conservative) values selected from the data evaluated. These endpoints provide protection from potential exposure for other species that are sensitive to nicosulfuron.

Toxicity studies with nicosulfuron indicated no adverse acute, dietary or reproductive effects on terrestrial invertebrates, birds or mammals. Nicosulfuron has adverse toxicological effects on terrestrial plants. Seedling emergence and vegetative vigour studies conducted on 22 plant species indicated that nicosulfuron inhibits seedling emergence and vegetative vigour. Contact with nicosulfuron arrests cell division and plant growth by inhibiting branched chain amino acid biosynthesis, which interferes with the enzyme acetolactate synthase (ALS). There were no toxicity studies available for review on the effects of transformation products of nicosulfuron on seedling emergence and vegetative vigour.

The screening level assessment indicated that the risk from exposure to nicosulfuron is well below the level of concern for terrestrial invertebrates, mammals and birds. Table 3 (Appendix X) summarizes the risk assessment for terrestrial organisms.

Nicosulfuron, being a herbicide, is a risk to non-target terrestrial plants. The level of concern (i.e. RQ = 1) for non-target terrestrial plants was exceeded by a maximum of 50 times. As a result, the risk assessment was refined taking into consideration the concentrations of nicosulfuron from spray drift that could occur in terrestrial habitat adjacent to the application site. For applications of nicosulfuron in the field, spray equipment uses the American Society of Agricultural Engineers (ASAE) medium spray droplet size. Based on this droplet size a maximum of 6% of the application will drift one metre downwind from the application site. Using this value, the EECs resulting from spray drift of nicosulfuron off site were calculated and the risk quotients ($RQ = EEC/EC_{25}$) were determined for nontarget terrestrial plants. Based on this method of refinement, the risk from nicosulfuron to nontarget terrestrial plants is reduced to a maximum of three times the level of concern from 50 times the level of concern. To mitigate the risk of nicosulfuron to non-target terrestrial plants, buffer zones will be required. Table 4 (Appendix X) summarizes the refined risk assessment for nicosulfuron to non-target terrestrial plants. The

buffer zones required to mitigate the risk to non-target terrestrial plants from the use of nicosulfuron are shown in Appendix XI.

4.2.2 Effects on Aquatic Organisms

The risk assessment for aquatic organisms is based on an evaluation of acute and chronic toxicity data for seven freshwater organisms including two species of invertebrates, three species of fish, one species of alga, and one species of macrophyte (vascular plant). There were no data available on estuarine/marine species. Toxicity data were also available for three of the eight major transformation products occurring in the aquatic environment and one of the minor transformation products. Aquatic toxicity data for nicosulfuron and its transformation products are summarized in Table 2 (Appendix X). The screening level risk assessment was carried out using the most sensitive toxicity endpoints from the range of toxicity data available, thereby providing a conservative assessment of the risk. The toxicity endpoints provide protection from potential exposure for other species that may be sensitive to nicosulfuron.

Acute and chronic toxicity tests indicate that nicosulfuron is toxic to sensitive species of freshwater fish and invertebrates but not to all species tested. The toxicity is increased by an order of magnitude with the presence of surfactants. Surfactants are used in the formulated products of nicosulfuron to disperse the active ingredient. The transformation products of nicosulfuron are not toxic to freshwater fish or invertebrates. There are no data available for estuarine/marine species. The acute toxicity of nicosulfuron to aquatic macrophytes and algae is about an order of magnitude greater than for fish and invertebrates. The presence of surfactants reduces the toxicity to aquatic macrophytes by about an order of magnitude, the opposite of the effect on fish and invertebrates. Nicosulfuron reduces biomass, growth rate, frond count and causes mortality in duckweed (*Lemna gibba*). In alga it reduces healthy cell count and growth rate. The transformation products of nicosulfuron did not have adverse effects on aquatic macrophytes (*Lemna gibba*) at the concentrations tested. Some toxic effects were observed with algae.

The risk assessment of nicosulfuron and its transformation products for aquatic life was carried out using data from the most sensitive freshwater organisms tested *Daphnia magna* (water flea), *Chironomus riparius* (benthic species), rainbow trout (*Oncorhynchus mykiss*), carp *(Cyprimus carpio*), zebra fish (*Bracydanio rerio*), duckweed (*Lemna gibba)* and the green alga *(Selenastrum capricornutum*).

The screening level risk assessment indicated that nicosulfuron and its transformation products are not a risk to freshwater invertebrates, fish, amphibians (based on surrogate data from fish studies), aquatic macrophytes and algae. The risk quotients were well below the level of concern (RQ = 1) for aquatic life. Therefore, no further refinement to the aquatic risk assessment was required. Since the highest concentration of nicosulfuron detected in monitoring studies of runoff was 3 orders of magnitude lower than the concentrations in the screening level risk assessment, no risk is expected from runoff. The risk assessment for nicosulfuron and its transformation products to aquatic organisms is summarized in Table 5 (Appendix X).

5.0 Value

5.1 Commercial Class Products

All nicosulfuron uses are supported by the registrant. There are no risk concerns for any of the registered uses. Consequently, no alternatives to the use of nicosulfuron is considered.

5.2 Domestic Class Products

There are no Domestic Class products containing nicosulfuron registered in Canada.

5.3 Value of Nicosulfuron

Quackgrass is one of the most troublesome and difficult to control weeds. A recent survey estimated that about 56% of Canadian farmland has quackgrass present. It can reduce corn yields by as much as 25 to 85%. Nicosulfuron is one of few herbicides that effectively control quackgrass in corn (including field, sweet and seed corn).

In Canada, the estimated average annual losses caused by weeds in the early 1990s were $54.4 million in field corn, $2.6 million in sweet corn, and $2.8 million in blueberry. Nicosulfuron was reported to be used in these crops to prevent and reduce a portion of the economic losses caused by weeds. In addition, nicosulfuron (co-formulated with rimsulfuron) is the only herbicide registered for the control of black bulrush in lowbush blueberry.

When used in field corn, the application window of nicosulfuron is wider (1–8 leaf stage for corn) than that of alternative non-sulfonylurea postemergent grass herbicides (spike to 2- or 3-leaf stage for corn).

The development of herbicide resistance in weeds associated with the use of nicosulfuron must be considered. Due to the widespread and frequent use of ALS inhibiting (Group 2) herbicides such as nicosulfuron; and lack of rotation with herbicides with other modes of action, more resistant weed biotypes have been documented in Canada with Group 2 herbicides than with any other herbicide group, including 12 broadleaf weeds (cleavers, chickweed, hemp-nettle, kochia, lamb's-quarters, giant ragweed, ball mustard, wild mustard, redroot pigweed, Russian thistle, spiny annual sowthistle, and stinkweed) and two grassy weeds (green foxtail and wild oats). Nevertheless, nicosulfuron still plays a role in mitigating resistance development in weeds to other herbicide groups.

6.0 Toxic Substances Management Policy Considerations

The federal government's *Toxic Substances Management Policy* provides guidance on the management of toxic substances, including preventive and precautionary approaches to dealing with substances entering the environment which could harm the environment or human health. The policy gives direction to decision makers and provides a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination of substances that are referred to in the policy document as Track 1 substances. These are toxic substances produced by human activity that are persistent and bioaccumulative.

During the environmental review, nicosulfuron was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of nicosulfuron were also considered, including major transformation products formed in the environment, microcontaminants in the technical active and formulants such as surfactants in the end-use products. In this regard the PMRA has reached the following conclusions:

- The *n*-octanol–water partition coefficient (log K_{ow}) of nicosulfuron is -4.63, which is well below the TSMP Track 1 cut-off criterion for log $K_{ow} \geq 5.0$. In addition, nicosulfuron does not meet the criteria for persistence, except possibly in anaerobic soils under low temperature conditions (e.g. 5 °C). Its half-life values in aerobic soils (17–150 days) and aerobic and anaerobic water-sediment systems (16–102 days) are below the TSMP Track 1 cut-off criteria for soil (≥182 days), water (≥182 days) and sediment (≥182 days). In anaerobic (flooded) soils, the half-life is variable and persistence is possible under low temperature conditions (63–1403 days). However, these conditions are unlikely to occur for extended periods of time during the period when it is used in Canada. The half-life of the major transformation products of nicosulfuron in soil range from two days (ADMP) up to 276 days (ASDM). Other studies with ASDM indicate half-life values of 92 and 113 days.

In conclusion, the use of nicosulfuron is not expected to result in the entry of Track 1 substances into the environment.

7.0 Summary

7.1 Human Health and Safety

7.1.1 Occupational Risk

Risk estimates associated with mixing, loading and applying nicosulfuron for proposed label uses are not of concern provided the recommended personal protective equipment is used. Postapplication exposure risks to re-entry workers are also not of concern provided the precautions and directions for use are followed.

7.1.2 Dietary Risk from Food

Chronic dietary risk assessments demonstrate no dietary concerns for any population subgroup in Canada, including infants, children, teenagers, adults and seniors. In addition, no dietary concerns were evident for nursing or pregnant females or based on gender in general.

7.1.3 Dietary Risk from Drinking Water

The potential for the contamination of drinking water with nicosulfuron is expected to be negligible. There are no drinking water concerns for any population subgroup in Canada, including infant, children teenagers, adults and senior.

7.1.4 Residential Risk

There are no domestic uses of nicosulfuron registered in Canada. Risks to homeowners from contact with commercially treated plants do not pose a health concern.

7.1.5 Aggregate Risk

Aggregate risks from food and drinking water are < 1% of the ADI and are not of concern.

7.2 Environmental Risk

Nicosulfuron is non-persistent in aquatic systems and soils except possibly in terrestrial soils under anaerobic (low oxygen) conditions. One of its major transformation products is more persistent than the parent compound but the risk from transformation products were below the level of concern. Nicosulfuron is potentially mobile in the environment. It may occur in runoff to nearby ponds, streams and rivers at very low concentrations. Runoff is usually greatest after a heavy or sustained rainfall on steeper slopes with compacted soils lacking vegetation. A screening level risk assessment indicates that it is not a risk to aquatic organisms, even if it is directly applied to water. Since the highest concentration of nicosulfuron detected in monitoring studies of runoff was three orders of magnitude lower than the concentrations in the screening level risk assessment, runoff is not expected to be a concern for aquatic life. Nicosulfuron use is not a concern for terrestrial organisms except for terrestrial plants. The risk assessment for non-target terrestrial plants indicates that spray drift will have adverse effects on non-target plants. However, these effects can be mitigated by the regulatory actions indicated below.

7.3 Value

Nicosulfuron controls quackgrass and many annual grassy weeds in corn at a low application rate.

Nicosulfuron reduces a portion of the economic losses caused by weeds estimated at $59.8 million in the early 1990s for field corn, sweet corn and blueberry. Nicosulfuron (co-formulated with rimsulfuron) is the only herbicide registered for the control of black bulrush in lowbush blueberries. Compared to alternative non-sulfonylurea postemergent grass herbicides, nicosulfuron has greater flexibility in application timing and is applied at a low rate which lessens the chemical load in the environment. Although nicosulfuron plays a role in mitigating resistance development in weeds to other herbicide groups, consideration has to be given to resistance management as more weed species are reported to be resistant to herbicides that inhibit acetolactate synthase (such as nicosulfuron) than to herbicides having other modes of action.

8.0 Proposed Re-evaluation Decision

The PMRA has determined that nicosulfuron is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and environment. As a condition of the continued registration of nicosulfuron uses, new risk reduction measures must be included on the labels of all products. No additional data are being requested at this time.

8.1 Proposed Regulatory Action Related to Human Health

The PMRA has determined that the dietary and drinking water risks, as well as worker risks during mixing, loading and application are acceptable for all uses, provided that the mitigation measures listed in Appendix XI are implemented.

8.1.1 Residue Definition for Risk Assessment and Enforcement

Division 15, Table II, of the Food and Drug Regulations currently identifies nicosulfuron (2[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino] sulfonyl]-*N,N*-dimethyl-3-pyridinecarboxamide) as the residue for risk assessment and enforcement. This residue definition is consistent with that of the USEPA. ([3-pyridinecarboxamide, 2-((((4,6-dimethoxypyrimidin-2-yl)aminocarbonyl)aminosulfonyl))-N,N-dimethyl]).

8.1.2 Maximum Residue Limits for Nicosulfuron in Food

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to update Canadian maximum residue limits and to remove MRLs that are no longer supported.

As shown in Table 8.1.2, the Food and Drug Regulations specify MRLs for nicosulfuron residues in blueberries. Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specified MRL (i.e. corn) must not exceed the general MRL of 0.1 ppm.

Where no specific MRL for a pest control product has been established in the Food and Drug Regulations, subsection B.15.002(1) applies. This requires that residues do not exceed 0.1 ppm and has been considered a general MRL for enforcement purposes. Currently, residues of nicosulfuron in all agricultural commodities, including those approved for treatment in Canada are regulated by subsection B.15.002(1). However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*.

Extrapolation of available residue data for corn following good agricultural practices (GAP), as described by the current product labels, indicated that residues would not exceed the limit of quantitation of the analytical method of 0.05 ppm. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set for blueberries and corn.

Table 8.1.2 Nicosulfuron MRLs for Commodities Approved in Canada

Commodity	MRL (ppm)
Blueberry	0.05
Corn	0.1*

* By virtue of subsection B.15.002(1) of the Food and Drug Regulations, the maximum residue limit of foods for which MRLs have not specifically been established is 0.1 ppm.

For supplemental MRL information regarding the International situation and trade implications, refer to Appendix XII.

8.2 Proposed Regulatory Action Related to Environmental Risks

The risk assessment of nicosulfuron indicates that adverse effects on non-target terrestrial plants are anticipated. To reduce the adverse effects of nicosulfuron in the environment, mitigation in the form of precautionary label statements and buffer zones are required. Environmental mitigation statements are listed in Appendix XI.

List of Abbreviations

a.i.	active ingredient
ADI	acceptable daily intake
AHAS	acetohydroxyacid synthase
ALS	acetolactate synthase
ARfD	acute reference dose
ASAE	American Society of Agricultural Engineers
atm	atmospheres
bw	body weight
CFIA	Canadian Food Inspection Agency
cm	centimetre(s)
DEEM®	Dietary Exposure Evaluation Model
DER	Data Evaluation Report
DFR	dislodgeable foliar residue
DNA	deoxyribonucleic acid
DT_{50}	dissipation time to 50% (the dose required to observe a 50% decline in the test population)
DWLOC	drinking water level of comparison
EC_{25}	exposure concentration to 25% (a concentration causing 25% adverse effects in the test population
EC_{50}	exposure concentration to 50% (a concentration causing 50% adverse effects in the test population
EChE	erythrocyte cholinesterase
EEC	expected environmental concentration
EP	end-use product
EXAMS	Exposure Analysis Modeling System
F/P/T	Canadian Federal, Provincial, and Territorial Committee
F_0	parental animals
F_1	first filial generation
g	gram(s)
GAP	good agricultural practice
GC-FPD	Gas Chromatography-Flame Photometric Detector
GC-MSD	Gas Chromatography-Mass Selective detector
GC-NPD	Gas Chromatography-Nitrogen Phosphorous Detector
h	hour(s)
ha	hectare(s)
Hg	mercury
IRED	Interim Reregistration Eligibility Decision (USEPA Document)
K_d	adsorption coefficient
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50% (a concentration causing 50% mortality in the test population
LD_{50}	lethal dose to 50% (a dose causing 50% mortality in the test population)
LOAEL	lowest observed adverse effect level
LOC	level of concern

LOD	limit of detection
LOEC	lowest observed effect concentration
m	metre(s)
m/sec	metre(s) per second
m^3	metre(s) cubed
mg	milligram(s)
µg	microgram(s)
mL	millilitre(s)
mm	millimetre(s)
MOE	margin of exposure
mv	millivolt(s)
MWHC	maximum water holding capacity
nd	no detection
NIO	nicosulfuron
nm	nanometre(s)
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
OC	organic carbon
OM	organic matter
PChE	plasma cholinesterase
PCP	Pest Control Product
PDP	Pesticide Data Program (United States data)
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
PRZM	Pesticide Root Zone Model
PSI	pre-slaughter interval
Q_1^*	cancer potency factor
REI	restricted-entry interval
Rf	retardation factor in chromatography
RQ	risk quotient
TC	transfer coefficient
TGAI	technical grade active ingredient
TP	transformation product
TPM	triophanate-methyl
TSMP	Toxic Substances Management Policy
URMULE	User Requested Minor Use Label Expansion
US	United States of America
USEPA	United States Environmental Protection Agency
USGS NAWQA	United States Geological Survey National Water-Quality Assessment Program
wk	week
°C	degree(s) Celsius

Appendix I Registered Nicosulfuron Products as of 14 July 2006

Registration Number	Marketing Class[1]	Registrant	Product Name	Formulation Type	Guarantee (%)[2]	
					NIO	DPY
23516	T	E.I. du Pont Canada Company	Nicosulfuron Technical Herbicide	Solution	93	—
23654	M		Nicosulfuron 75 DF Manufacturing	Wettable granules	75	—
24682	C		Ultim Herbicide 37.4% Dry Flowable		18.7	18.7
24736	C		Ultim Herbicide 75% Dry Flowable		37.5	37.5
25116	C		Accent 75% DF Herbicide		75	—
26676	M		Ultim 75 DF MUP		37.5	37.5

1 T = Technical active; M = Manufacturing concentrate; C = Commercial.

2 DPY = rimsulfuron; NIO = nicosulfuron; — = not included.

Note: Discontinued products or products with a submission for discontinuation are not included.

Appendix II Registered Uses of Nicosulfuron as of 14 July 2006 [1]

Use Site Category	Sites		Weeds[2]	Maximum Application Rate	Use Supported?[3]
13, 14 Terrestrial feed crops and terrestrial food crops	Field corn	Eastern Canada	A	12.6 plus rimsulfuron at 12.6 (co-formulation)	Y
			Long-spined sandbur		M
			B	25	Y
		Western Canada - Manitoba, Saskatchewan, Alberta,	B plus wild oats	25	M
		Manitoba	A	12.6 plus rimsulfuron at 12.6	M
	Sweet corn	Eastern Canada and Western Canada	B	25	M
	Seed corn inbreds	Eastern Canada			
14 Terrestrial food crops	Lowbush blueberries	Eastern Canada	Black bulrush	12.6 plus rimsulfuron at 12.6	M

[1] The formulation type for all supported end-use products is wettable granules. Application is made once per year by ground equipment only. No aerial application is allowed for any uses. Information on application equipment and the number of applications is based on both label use information and information provided by the registrant under DACO 5.2. Uses of tank-mix products including the prepackaged tank mixes are not presented.

[2] A = Barnyard grass, fall panicum, green foxtail, proso millet, quackgrass, redroot pigweed (including triazine resistant), yellow foxtail (suppression), and old witchgrass

B = Barnyard grass, fall panicum, green foxtail, old witchgrass, quackgrass, yellow foxtail (suppression)

[3] Y = Use is currently registered and supported by the registrant.

M = Use was added to the use pattern as a User Requested Minor Use Label Expansion and is supported by the registrant.

Appendix III Toxicology Profile for Nicosulfuron

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise specified.

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Metabolism/Toxicokinetic Studies		
Metabolism study (absorption, distribution, metabolism, excretion) of pyridine-2-^{14}C- and pyrimidine-2-^{14}C-nicosulfuron—Crl:CDBR rat		Absorption: rapid absorption (based on the rate of excretion) Distribution: Minimal residual tissue activity (0.050–0.25% of the administered oral doses) Metabolism: Most of the radioactive nicosulfuron was excreted in an unchanged form (85%–97% of recovered radioactivity). A minor amount may be hydroxylated at the 5′ carbon on the pyrimidine portion of the molecule then hydrolytically cleaved to yield pyridine sulfonamide and 5-hydroxy pyrimidine amine. Alternatively pyrimidine amine may be hydroxylated at the 5 position following hydrolytic cleavage Excretion: The majority of the administered dose was excreted in 24 hr (>80%). Low oral dose: 12–18% (urine) and 67–81% (feces) excreted in 24 hours; 13–20%(urine) and 81–88% (feces) excreted after 3 days. High oral dose: 8–10% (urine) and 78–92% (feces) excreted in 24 hr; 9–11% (urine) and 89–95% (feces) excreted after 3 days.
Metabolism study (absorption, distribution, metabolism, excretion) of pyridine-2-^{14}C-nicosulfuron—BRL-HAN Wistar rat		Absorption: rapidly absorbed at both high and low doses Distribution: mean tissue residues in all groups were low (0–0.2%) Metabolism: a) Fecal extract (59.8–79.6% of administered radioactivity): Nicosulfuron excreted largely unchanged (49.5–73.6%). Two fecal metabolites were identified - HMUD (1.6–2.9%) and ASDM (1.8–2.3%). Five additional fecal metabolites were isolated but not identified (≤1–4%) b) Urine (13.8–34.0% of administered radioactivity): Nicosulfuron excreted largely unchanged (10.1–22.1%). Four urinary metabolites were identified - HMUD (0.2–0.5%), ASDM (2.6–9.2%), UCSN (0.1–0.3%) and AUSN (≤0.3%). Three additional urinary metabolites were isolated but not identified (≤1–2.6%) c) Bile (13.1–14.0% in bile duct cannulated animals): Three compounds in the bile - unchanged nicosulfuron (12.1–13.2%), HMUD (0.2–0.5%), unidentified metabolite (0.3–0.8%) Excretion: 61.8–82.4% in feces, and 13.8–34.6% in urine within 72 hours; biliary contribution to fecal excretion was 20.1% in males and 23.9% in females

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Metabolism study (absorption, distribution, metabolism, excretion) of pyrimidine-2-^{14}C-nicosulfuron—BRL-HAN Wistar rat		Absorption: rapidly absorbed at both high and low doses. Distribution: mean tissue residues in all groups were found to be low (0–0.1%) Metabolism: a) Fecal extract (53.4–67.1% of administered radioactivity): Nicosulfuron excreted largely unchanged (53.4–69.0%). Three fecal metabolites were identified - ADMP (1.4–1.7%), HMUD (0.5–1.2%) and AHDP (0.2 –0.5%). b) Urine (14.1–30.5% of administered radioactivity): Nicosulfuron excreted largely unchanged (14.1–30.5%). Four urinary metabolites were identified - HMUD (0.2–0.4%), ADMP (0.2–0.4%), AHDP (2.9–8.0%) and 5-HDUD (0.1%). Two additional urinary metabolites were isolated but not identified (≤1–2.3%) c) Bile (13.8–15.8% in bile duct cannulated animals): Five compounds in the bile - unchanged nicosulfuron (11.9 –13.1%), HMUD (0.4-0.5%), unidentified metabolites (1.4–2.3% total) Excretion: 57.9–72.9% in feces, and 17.9–41.2% in urine within 72 hours; biliary contribution to fecal excretion was 23.0% in males and 26.2% in females
Acute Toxicity Studies		
Acute oral toxicity—mouse		LD_{50} > 5000 mg/kg bw **LOW TOXICITY**
Acute oral toxicity—rat		LD_{50} > 5000 mg/kg bw **LOW TOXICITY**
Acute dermal toxicity—rat		LD_{50} > 2000 mg/kg bw Pigmented orbital secretion (3/10) on days 1 and 2; accompanied by bulging eyes in 2/10. **LOW TOXICITY**
Acute dermal toxicity—rabbit		LD_{50} > 2000 mg/kg bw Slight weight loss within 24 hrs., recovery by day 7. Slight to severe erythema (5/10), mild edema (1/10); no dermal irritation by day 4. **LOW TOXICITY**
Acute inhalation toxicity—rat		LD_{50} > 5.47 mg/L Slight to severe bw losses one day after exposure; some experienced slight to moderate losses during second week. **LOW TOXICITY**
Eye irritation—rabbit		Slight corneal opacity and mild conjunctival redness in 6/6, moderate iritis and slight chemosis in 5/6 (mild chemosis in 1/6); no corneal injury, all treated eyes normal by day 3. Mean scores: 28.5 (1 hr); 2.3 (24 hr); 0.7 (48 hr); 0 (72 hr) **MODERATELY IRRITATING**
Dermal irritation—rabbit		**NON-IRRITATING**
Dermal sensitization - Guinea pig		**POTENTIAL SKIN SENSITIZER**
Subchronic Toxicity Studies		
2-week oral (gavage) —mouse	≥2200	no treatment-related effects
6-week oral (feeding) —mouse	782	7761/9703 mg/kg bw/day: ↓bw gain (24% - ♂), ↓food consumption (12% during first week of study only - ♂)

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
90-day oral (feeding) —mouse	≥1441	no treatment-related effects
2-week oral (gavage) —rat	≥2200	no treatment-related effects
4-week oral (feeding) —rat	≥2200	4782/5152 mg/kg bw/day: ↓bw gain(19% - ♀), slightly ↓food consumption (4% - ♀), ↑α-1 globulin (and ↓albumin:globulin ratio)(♂ - but within historical range)
90-day oral (feeding) —rat	≥1441	no treatment-related effects
90-day oral (feeding) —rat	358	3672/4230 mg/kg bw/day: slightly ↓bw (4% - ♂, 6% - ♀ -not significant), slightly ↓platelet numbers (♂)
4-week oral (capsules) —Beagle dog	200	2000 mg/kg bw/day: ↑enzyme activity indicative of hepatotoxicity [ALT (48%), γ-glutamyl transpeptidase (43%), ornithine carbamoyl transferase (21%) - ♂], slightly ↑platelets (1♂ and 1♀), slightly ↑relative liver weight (24% - 1♂)
90-day oral (feeding) —Beagle dog	≥656	no treatment-related effects
90-day oral (capsules) —Beagle dog	200	2000 mg/kg bw/day: ↓bw gain (♀ - 24%), ↓food consumption (♀ - 3%), ↑enzyme activity indicative of hepatotoxicity [ALT - minimally ↑ in ♀ at 12 weeks and significantly ↑(134%) in a ♀ exhibiting significantly ↓ bw gain, ornithine carbamoyl transferase - slightly ↑(19%) at 12 weeks (♂)], ↑relative liver weight (23% - ♂, 1♀ had high liver weight - 135% of control), ↑relative thyroid weight (44% - ♂).
1-year oral (feeding) —Beagle dog	141/≥563.5	571/563.5 mg/kg bw/day (20,000 ppm): ↓bw (11%)/bw gains (41%) (non-significant - ♂), ↑liver and kidney weights (rel. - absol. liver weights as well, but not significant) (♂)
1-year (capsules) —Beagle dog	200	2000 mg/kg bw/day: ↑enzyme activity [AP - ♂ at 24 weeks (61%) and 50 weeks (70%), also ♀, but not significantly], slightly ↑ BUN (♀ at 24 weeks), ↑creatine phosphokinase at 24 weeks in 1 ♂ (within control range at 50 weeks)
Chronic Toxicity/Oncogenicity Studies		
18-month feeding study—mouse	≥953	no treatment-related effects **No evidence of oncogenicity**

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
2-year feeding study—mouse	544	6183/5818 mg/kg bw/day: ↓bw (♂ - consistently lower throughout study period), ↓bw gain (♂ - 9% overall), slight ↑food consumption (♂), slight ↑ liver weights (♂ - not sig.; absol. - 10%, rel. - 11%), ↑incidence of distended gall bladder (♀), ↑incidence liver masses (♂), ↑incidence hepatocellular carcinomas (♂ - sig., but within historical range and controls low)*, ↑incidence hepatocellular adenomas (♂ - not sig., but slightly outside historical range)*, ↑incidence malignant lymphomas (♀ - sig.)** *Increased incidence of hepatocellular tumours is only seen at a very high dose level greatly in excess of current recommended maximum (1000 mg/kg bw/day) and is therefore not considered relevant to human risk assessment. **Increased incidence of malignant lymphomas in female mice is likely a reflection of the very high dose used. The difference from the historical control range is marginal (32.7% vs. 28%), and USEPA has noted that this tumour occurs spontaneously in this sex and strain of mice. **Not carcinogenic**
2-year feeding study—rat	≥786	no treatment-related effects **No evidence of oncogenicity**
2-year feeding study—rat	199	2087.5/2622.7 mg/kg bw/day: ↓bw gain (♂ 0–52 wks - 5%, 0–78 wks - 15%;♀ 1–52 wks - lower but not sig.), slight ↓food consumption (♀ 1–13 wks only), slight ↓ Hgb, RBC and PCV (♂ wks 50 and 76), ↑plasma urea [♀ wks 24 (31%) and 50 (29%); ♂ wk 76 (92%)], ↑ovary wt. (absol. and rel.), ↑ incidence pancreatic aneurysmal ateritis (♂), ↑ renal pelvis mineralization (♀) **No evidence of oncogenicity**
Reproductive and Developmental Toxicity Studies		
Two-generation reproduction feeding study—rat	Parental, Reproduction, and Offspring: ≥1263	no treatment-related effects
Two-generation reproduction feeding study—rat	Parental: ≥3302/ 369.9 Reproduction and Offspring: ≥3302	3302-3861/3719-4404 mg/kg bw/day: ↓bw gain[F_0 ♀ (wks 1–11), F_1 ♀ (wks 0-14)], slight ↓ food consumption (F_1 ♂ during first week)
Developmental study (gavage)—rat	Maternal and Developmental: ≥6000	no treatment-related effects **No evidence of teratogenicity.**

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
Developmental study (gavage)—rat	Maternal and Developmental: ≥1000	no treatment-related effects **No evidence of teratogenicity.**
Developmental study (gavage)—rabbit	Maternal: 100 Developmental: 1000	≥500 mg/kg bw/day: clinical signs (altered fecal excretion and discharge), ↓bw gain, ↓food consumption, ↑abortions*, ↑mortality* *Abortions and Deaths: The increase in abortions and in mortality does not appear treatment related (except at the high dose which exceeds our limit dose). Historical controls (1980–1984 Argus Labs) indicated 0–1 deaths and 0–2 abortions per group. Number of deaths exceeded these historical control values only at 2000 mg/kg bw/day which exceeds the current limit dose of 1000 mg/kg bw/day. The number of abortions slightly exceeded historical controls at 500 mg/kg bw/day (3), but was within historical control values at 1000 mg/kg bw/day (2). **No evidence of teratogenicity.**
Developmental study (gavage)—rabbit	Maternal: 300 Developmental: ≥600	600 mg/kg bw/day: ↑mortality (abnormal/haemorrhagic intestinal contents in one animal killed *in extremis* on day 10; another animal found dead on day 17), orange/red staining of hocks and cage undertray (10/15 animals during and immediately following treatment period) Number of deaths slightly exceeded historical controls at 600 mg/kg bw/day, (2 vs. 1) however numbers of deaths were within historical controls (0-1) at 500mg/kg bw/day and 1000 mg/kg bw/day in two other rabbit developmental studies. **No evidence of teratogenicity.**
Genotoxicity Studies		
Ames reverse mutation test—*Salmonella typhimurium* TA1535, TA97, TA98, TA100)	**Negative**	
Ames reverse mutation test—*Salmonella typhimurium* TA1535, TA1537, TA98, TA100)	**Negative**	
Bacterial DNA repair test (Rec-assay) - *Bacillus subtilis* H17, rec^+, M45, rec^-	**Negative**	
In vivo bone marrow micronucleus assay - Crl:CD-1 (ICR)BR mice	**Negative**	

Study/Species/ # of Animals per Group	NOAEL (mg/kg bw/day)	Results/Effects
In vivo bone marrow micronucleus assay - BDF1 mice	**Negative**	
In vitro unscheduled DNA synthesis assay in rat primary hepatocytes	**Negative**	
Unscheduled DNA synthesis in rat hepatocytes - ♂ CD rats	**Negative**	
In vitro chromosome aberrations in human lymphocytes	**Negative**	
CHO/HPRT assay	**Negative**	
In vitro cytogenetics test - Chinese hamster lung (CHL) cells	**Negative**	

Appendix IV Toxicology Endpoints for Health Risk Assessment for Nicosulfuron

Exposure Scenario	Dose (mg/kg bw/day)	Endpoint	Study	UF/SF or MOE[a]
Acute dietary	An acute reference dose was not calculated since there was not an endpoint of concern			
Chronic dietary	NOAEL = 141.1	Decrease in body weight and body-eight gain (♂), increase in relative liver and kidney weights (♂)	1-year feeding study—dog	100
	ADI = 1.41 mg/kg bw/day			
Short[b]-, intermediate[c]- and long[d]-term oral, dermal and inhalation[e]	NOAEL = 141.1	Decrease in body weight and body-eight gain (♂), increase in relative liver and kidney weights (♂)	1-year feeding study—dog	100
Cancer	non-carcinogenic			

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments, MOE refers to desired margin of exposure for occupational or residential assessments

[b] Duration of exposure is 1–30 days

[c] Duration of exposure is 1–6 months

[d] Duration of exposure is > 6 months

[e] Because an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation

Appendix V Summary of Occupational Exposure Risk Estimates for Nicosulfuron

Table 1 Route Specific MOEs for Mixers/Loaders/Applicators of Products Containing Nicosulfuron

Crop	Method of Application	Formulation[a]	Application Rate[b]	Area Treated per day[c]	Margins of Exposure		
					Dermal[d]	Inhalation[e] no resp.	Combined[f] no resp.
Baseline PPE : long sleeved shirt, long pants, with chemical resistant gloves; closed M/L; open cab application without gloves (if applicable)					Target MOE = 100		
Corn (Field, Seed, Sweet)	Groundboom	WG in WSP	0.025 kg a.i./ha	Farmer : 100 ha	20 080	1 995 354	19 880
				Custom : 300 ha	6 693	665 118	6 627
				Farmer : 100 ha	80 045	3 720 151	78 359
				Custom : 300 ha	26 682	1 240 050	26 120
Lowbush Blueberries	Backpack	WG in WSP	0.000016 kg a.i./L	Farmer and Custom: 150 L	767 693	67 322 717	759 038
	Low pressure handwand				4 431 708	92 494 264	4 229 079

[a] WG = Wettable granule, WSP = Water soluble package

[b] Maximum label rate.

[c] Default ATPD values. For lowbush blueberries, assumed same volume applied for farmers and custom applicators based on limitations of equipment.

[d] Dermal MOE = dermal NOAEL/dermal exposure. The short- and intermediate-term dermal NOAEL is 141.1 mg/kg bw/day. Dermal exposure (µg/kg bw/day) = (dermal unit exposure (µg/kg ai) × area treated per day × application rate × DA)/body weight. (DA = dermal absorption of 100%, Body Weight = 70 kg)

[e] Inhalation MOE = inhalation NOAEL/inhalation exposure. The short- and intermediate-term inhalation NOAEL is 141.1 mg/kg bw/day. Inhalation exposure (µg/kg bw/day) = (Inhalation unit exposure (µg/kg a.i.) × area treated per day × application rate)/body weight). Body weight = 70 kg.

[f] Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$

Table 2 Postapplication Exposure Estimates for Re-entry Into Fields Treated With Nicosulfuron

Crop and Rate (kg a.i./ha)	Number of Applications per year	Activity	Transfer Coefficient [a] (cm^2/hr)	Calculated DFR [b] at Day 0 (µg/cm^2)	Exposure [c] (µg/kg bw/day)	MOE [d]
Use-site Categories 13 and 14: Terrestrial Feed and Food Crops						**Target = 100**
Corn (Field, Seed, Sweet) Rate: 0.025	1	Full Foliage: Hand Detasseling, Hand Harvesting, Hand Weeding, Irrigation, Scouting	17 000	0.05	97.14	1 453
			1 000	0.05	5.71	24 693
		Minimum Foliage: Scouting, Hand Weeding	400	0.05	2.29	61 731
			100	0.05	0.57	246 925
Lowbush Blueberries Rate: 0.0126	1 assumed Multiple applications permitted	Full Foliage: Hand harvesting, Hand pruning	1 500	0.025	4.32	32 662
		Full and/or Minimum Foliage: Irrigation, Thinning, Hand pruning, Scouting, Hand weeding	400	0.025	1.15	122 483

[a] Transfer coefficients (TC) are from the Science Advisory Council for Exposure, Policy No. 003.1 (USEPA, 2000b) and any amendments thereof.

[b] DFR calculations are based on a peak default DFR value of 20% of the application rate and 10 % dissipation rate per day. Based on one application per season.

[c] Exposure = DFR × TC × 8 hr × DA/70 kg. (DA = dermal absorption of 100%)

[d] Based on worker short-term NOAEL of 141.1 mg/kg bw/day and target MOE of 100.

Appendix VI Dietary (Food and Water) Exposure and Risk Estimates for Nicosulfuron

Nicosulfuron		
Chronic exposure ADI = 1.41 mg/kg bw/day		
Population	**Exposure**	**% ADI**
Canadian Population (total)	0.00115	0.1
All infants (<1 year)	0.001894	0.1
Nursing infants	0.000587	0.1
Non-nursing infants	0.00239	0.1
Children 1–2 yrs	0.004653	0.2
Children 3–5 yrs	0.003312	0.3
Children 6–12 yrs	0.002054	0.1
Youth 13–19 yrs	0.001066	0.1
Adults 20–49 yrs	0.000745	0.1
Adults 50+ yrs	0.000656	0.1
Females 13–49 yrs	0.000735	0.1

Appendix VII Food Residue Chemistry Summary

1.1 Metabolism

The PMRA concluded that the residue chemistry database for nicosulfuron is largely complete. Nature and magnitude of the residue in plants and livestock are adequately understood. Conclusions from the European Food Safety Authority (2006), the Environmental Protection Agency (2004) and the United Kingdom Pesticides Safety Directorate (2000) are consistent with the PMRA's conclusion.

1.1.1 Plant Metabolism

The PMRA has reviewed nicosulfuron metabolism studies conducted on corn and canola and concluded that the qualitative and quantitative metabolic fate, transposition and disposition of nicosulfuron have been adequately demonstrated. Studies were conducted using radiolabelled forms (pyridine and pyrimidine rings) in order to investigate the fate of the two moieties of the compound. None of the metabolites formed is found to be of particular concern.

However, due to significant amounts of metabolites found in corn stalk (21 to 58% TRR) and canola foliage (16 to 28% TRR), the PMRA may require additional metabolism and residue studies if the registrant wishes to propose new uses on treated foliage crops (e.g. leafy vegetables). Based on the identification of the metabolites, the metabolism of nicosulfuron in plants proceeds via the cleavage of the sulfonylurea bridge resulting in the formation of pyridine sulfonamide and pyrimidine amine. A minor metabolic reaction occurs via the hydroxylation at the 5-position of the pyrimidine ring of nicosulfuron.

1.1.2 Livestock Metabolism

The PMRA has reviewed nicosulfuron metabolism studies conducted on lactating goat orally administered radiolabelled either pyridine or pyrimidine ring.

The proposed metabolic pathway for nicosulfuron in the goat showed three mechanisms:

1) hydrolysis of the sulfonylurea bridge to yield pyridine sulfonamide and pyrimidine amine (both of which undergo additional metabolism);
2) N-demethylation and subsequent loss of sulfur dioxide leading to the cyclized compound was identified as a "cyclized ipso compound,"; and
3) oxidation and conjugation at the 5-position of the pyrimidine ring.

Nicosulfuron and its metabolites were not found to accumulate in milk and meat.

1.1.3 Residue Definition

Based on metabolism studies which showed a rapid and extensive metabolism of nicosulfuron in the tested crops, the PMRA has determined that only the parent compound should be included in the residue definition for both regulation and risk assessment. The residue definition is consistent with that of other regulatory authorities such as the USEPA, EFSA, and the PSD.

Since livestock metabolism studies conducted at exaggerated dose rates showed no significant concentrations of nicosulfuron or its metabolites in meat and milk, and as no significant residues are expected to be present in corn products intended for livestock consumption, the PMRA concludes there is no need to propose a definition of residue for food of animal origin.

1.2 Analytical Methods

1.2.1 Methods for Residue Analysis of Plants and Plant Products

The PMRA has reviewed analytical methods for determination of residues of the parent compound in corn and blueberries. The recoveries in forage and grain using HPLC-UV were between 96–99% and 80–99%, respectively. An LC-MS/MS method was reviewed for determination of nicosulfuron residues in corn forage and grain with recoveries of 81–105 and 84–100%, respectively. As well, an HPLC-UV was reviewed for analysing residues of nicosulfuron in blueberries and was found acceptable based on good recoveries and low LOD of 0.016 ppm. For enforcement purposes, the analytical method reviewed for analysis of nicosulfuron residues was satisfactory based on the percentage of recovery and sensitivity of the method.

1.2.2 Methods for Residue Analysis of Food of Animal Origin

Based on ruminant expected maximum theoretical dietary burden which reported negligible residues, restrictions on labels which prevent feeding animals with treated crops and the absence of direct animal treatment use of nicosulfuron, there is no reasonable expectation of finite residues in livestock matrices. An analytical method for food of animal origin is not required. However, if the registrant wishes to support use of nicosulfuron involving direct livestock or poultry treatment, then residue analytical methods capable of determining nicosulfuron residues of concern in animal tissues, milk and eggs from direct treatments will be required.

1.2.3 Multiresidue Analytical Methods

The multiresidue method for fruits and vegetables of the CFIA does not list nicosulfuron as one of the pesticides that has been evaluated through the multiresidue protocols. As well, none of the US Food and Drug Administration multi-residue protocols (A to E) is applicable for the analysis of nicosulfuron. Multiresidue methods are not suitable for the analysis of nicosulfuron.

1.3 Food Residues

1.3.1 Storage Stability

The PMRA has reviewed freezer storage stability studies and concluded that nicosulfuron is stable in field corn for 24 months and up to eight months for sweet corn when stored frozen at approximately −20°C.

1.3.2 Crop Residues

The PMRA has reviewed supervised residue trial studies conducted on corn and blueberries. All these field trials conducted in Canada, United States and in Europe showed that all residues were below the LOQ of the analytical method (LOQ of 0.05 ppm). It is therefore considered that no significant residues of nicosulfuron will be detected on treated corn and blueberry when treated in accordance with the proposed label directions.

1.3.3 Livestock Residues

The PMRA has concluded that in the absence of finite residues of nicosulfuron in livestock food commodities and based on the fact that exaggerated dose rates used to conduct livestock metabolism studies showed no significant concentrations of nicosulfuron or its metabolites in meat and milk, residues are not expected in livestock. As well, no residues were detected in animal feed items when used according to directions specified on labels (which specify to avoid feeding animals with treated crop).

1.3.4 Confined Accumulation in Rotational Crops

The PMRA has concluded there is no reasonable expectation of residues of nicosulfuron and its metabolites after application to corn in rotational food crops and feed items when nicosulfuron is applied in accordance with good agricultural practices. Data from confined rotational crop studies conducted on lettuce, radish, soybean and wheat showed that nicosulfuron and its metabolites did not accumulate in rotational crops grown in soil treated at a maximum use rate of 70 g. Since blueberries are not considered a rotational crop, no rotational trials will be required for the continued registration of nicosulfuron.

Appendix VIII Water Monitoring Data

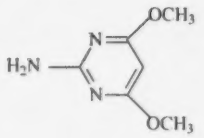
A search for existing water monitoring data in Canada revealed that routine analysis for nicosulfuron is not conducted. Water monitoring data for the sulfonylureas that are currently under re-evaluation was requested from provincial and territorial departments responsible for water quality monitoring. Monitoring data were also requested from Environment Canada, the Department of Fisheries and Oceans and the drinking water subcommittee through Health Canada. Although Environment Canada has begun to include monitoring data on the sulfonylureas as part of the Pesticide Science Fund, nicosulfuron is not included in the analysis.

Given the absence of monitoring data in Canada for residues of nicosulfuron in water, both the United States Environmental Protection Agency and the United States Geological Survey databases were searched for detections of nicosulfuron. Nicosulfuron was not included among the analytes that are sampled in either of these databases.

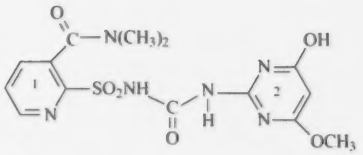
The only monitoring data available on nicosulfuron were from a study of sulfonyl urea herbicides in South Dakota rivers conducted by the South Dakota Department of Environment and Natural Resources in 2003. These data were not of sufficient quantity and quality to be utilized in the risk assessment. A total of 20 samples were collected and analyzed for several sulfonyl urea herbicides. Nicosulfuron was detected on six occasions in three of the five rivers sampled. Only one detection was above the limit of quantification (0.05 µg/L). The concentration was 0.061 µg/L. This value is several orders of magnitude below the level of concern. Five additional detections occurred at concentrations below the limit of quanitification but above the limit of detection (0.01 µg/L).

Appendix IX Major Transformation Products of Nicosulfuron

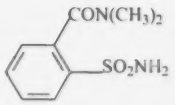
ADMP
2-amino-4,6-dimethoxypyrimidine
Occurs in soil (maximum 27% of applied parent)



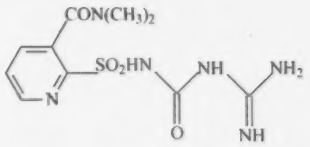
HMUD
2-(4-hydroxy-6-methoxypyrimidin-2-ylcarbamoylsulfamoyl)-N,N-dimethylnicotinamide. Occurs in soils, water and sediment (maximum in soil 18.5% of applied parent; in water and sediment 19.2% of applied parent)



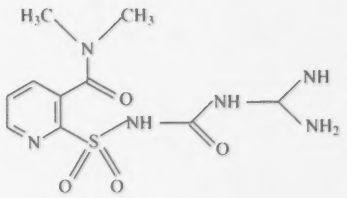
ASDM
N,N-dimethyl-2-sulfamoyl-nicotinamide
Occurs in soils, water and sediment (maximum in soil biotransformation studies 19% of applied parent; in soil phototransformation studies 23% of applied parent; in water and sediment 9.4% of applied parent)



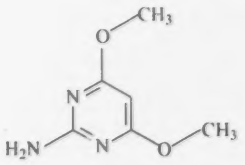
AUSN
2-(3-amidinoureidosulfonyl)-N,N-dimethylnicotinamide
Occurs in soil, water and sediment (maximum in water and sediment 11.1% of applied parent; no value indicated for soil)



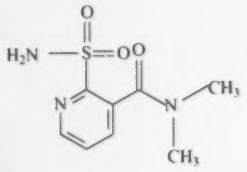
IN-HYY21
2-[[[[(aminoiminomethyl)amino]carbonyl]amino]sulfonyl]-N,N-dimethyl-3-pyridinecarboxamide. Occurs in aerobic soil (maximum 34% of applied parent)



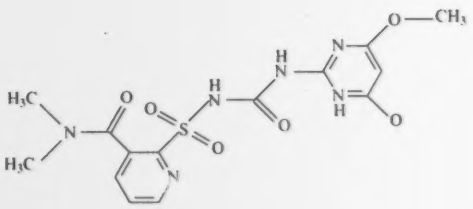
IN-J0290
CAS name: 4,6-dimethoxy-2-pyrimidinamine
(i.e. pyrimidine amine). Occurs in aerobic soil (maximum 49% of applied parent)



IN-V9367
2-(aminosulfonyl)-N,N-dimethyl-3-pyridinecarboxamide (i.e. pyridine sulfonamide). Occurs in aerobic soil (maximum 18.2% of applied parent)



IN 37740
O-Desmethyl Nicosulfuron
CAS name: 2-[[3,4-dihydro-6-methoy-4-oxopyrimidin-2-ylaminocarbonyl]aminosulfonyl]-N,N-dimethyl-3-pyridinecarboxamide).
Occurs in water in aquatic aerobic and anaerobic studies (maximum in water 29% of applied parent)



Appendix X Environmental Fate and Toxicity

Table 1 Environmental Fate of Nicosulfuron and its Transformation Products

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
Abiotic transformation					
Hydrolysis	Nicosulfuron	30 d, 25°C	DT_{50} pH 5 15 d DT_{50} pH 7 Stable DT_{50} pH 9 Stable	Major route of transformation under acidic conditions	Not reported
Phototransformation - soil	Nicosulfuron	Loam (pH 7.3)	DT_{50} 36–39 d	Not a major route of transformation	ASDM 23% AR
Phototransformation - water		25°C	DT_{50} pH 4.9 44–53 d DT_{50} pH 7.3 58–154 d DT_{50} pH 9.2 69–73 d	Not a major route of transformation	ASDM
Phototransformation - air	Nicosulfuron		0.6 h	Major route of transformation	Not reported
Biotransformation					
Soil - aerobic	Nicosulfuron	Sand OC 0.5%, pH 6 Sandy loam OC 0.7%, pH 6.6 Loam OC 1.5%, pH 5.5	DT_{50} 39–43 d DT_{50} 25–29 d DT_{50} 17–24 d	Moderately persistent Moderately persistent Slightly persistent	ADMP 27%, HMUD 19%
		Silt loam OC 1.4%, pH 6.1	DT_{50} 30–33 d	Moderately persistent	Not reported
		Silt loam OM 2.4%, pH 7.1	DT_{50} 22 d	Slightly persistent	IN-HYY21 19% IN-V9367 19%
		Sandy loam OM 1.8% pH 6.1 Sandy loam OM 2.8% pH 5.4 Sandy loam OM 2.8% pH 5.4 Loam OM 1.8% pH 7.5	DT_{50} 50 d 20°C DT_{50} 16 d 20°C DT_{50} 150 d 10°C DT_{50} 18 d 20°C	Moderately persistent Slightly persistent Moderately persistent Slightly persistent	IN-HYY21 34% IN-J0290 49%

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
	ASDM	Loamy sand, OC 1%, pH 7.6 Loamy sand, OC 2.3%, pH 6 Loam, OC 2%, pH 7.3	DT_{50} 2 d DT_{50} 5 d DT_{50} 7 d	Not persistent	CO_2
	ASDM	Loamy sand OC 1%, pH 7.6 Loamy sand OC 2.3%, pH 6 Loam OC 2.% pH 7.3	DT_{50} 92 d DT_{50} 276 d DT_{50} 113 d	Moderately persistent Persistent Moderately persistent	CO_2
	AUSN	Loamy sand OC 1%, pH 7.6 Loamy sand OC 2.3%, pH 6 Loam OC 2.% pH 7.3	DT_{50} 53 d DT_{50}>101 d DT_{50} 91 d	Moderately persistent Persistent Moderately persistent	Not reported
	UCSN	Loamy sand OC 1%, pH 7.6 Loamy sand OC 2.3%, pH 6 Loam OC 2.% pH 7.3	DT_{50} 128 d DT_{50}>100 d DT_{50}>100 d	Persistent	Not reported
Soil - anaerobic	Nicosulfuron	Silt loam OC 1.4% pH 6.1	Stable	Persistent	HMUD 15% ASDM 19%
		Soil properties not reported	DT_{50} 63 d 25°C DT_{50} 736-1403 d 5°C	Moderately persistent Persistent	IN-V9367 9.5%
Water/sediment - aerobic	Nicosulfuron	Loamy sand sed. OC 1.1% pH 6.9 Loamy sand sed. OC 1.4% pH 6.9	DT_{50} 38 d river water DT_{50} 37 d pond water	Moderately persistent	HMUD 19% AUSN 11% ASDM 9.4%
		pH 7.8, OM 2.1%	DT_{50} 83 d (80 d water layer only)	Moderately persistent	IN 37730 22–29% in water
		pH 8.2 OM 1.6%	DT_{50} 102 d (82 d water layer only)	Moderately persistent	IN 37730 15–17%% in water
Water/sediment-anaerobic	Nicosulfuron	Soil properties not reported	DT_{50} 15 d 25°C DT_{50} 85 d 5°C	Moderately persistent	Not reported

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
Mobility					
Adsorption/ desorption	Nicosulfuron	Loamy sand OC 0.5% pH 6 Loamy sand OC 2.5% pH 6 Silt loam OC 1.4% pH 7.7 Silt loam OC 1.4% pH 6.1	Koc 10 Koc 8 Koc 51 Koc 14	Very highly mobile	Not reported
	ADMP	Loamy sand OC 2.3% pH 7.7 Sandy loam OC 1.2% pH 7.8 Silt loam OC 4.1% pH 7.3	Koc 60 Koc 53 Koc 42	Very highly mobile	Not reported
	ASDM	Loamy sand OC 2.3% pH 7 Loamy sand OC 1.2% pH 7.7 Sandy loam OC 1.6% pH 7.8 Silt loam OC 4.1% pH 7.3	Koc 2.3 Koc 6.7 Koc 7.7 Koc 6.0	Very highly mobile	Not reported
	AUSN	Loamy sand OC 2.3% pH 7 Loamy sand OC 1.2% pH 7.7 Sandy loam OC 1.6% pH 7.8 Silt loam OC 4.1% pH 7.3	Koc 13 Koc 36 Koc 39 Koc 22	Very highly mobile	Not reported
	UCSN	Loamy sand OC 2.3% pH 7 Loamy sand OC 1.2% pH 7.7 Sandy loam OC 1.6% pH 7.8	Koc 1.1 Koc 5.6 Koc 1.1	Very highly mobile	Not reported
Soil column leaching	Nicosulfuron	2 loamy sand soils (OC 0.5% and 2.5%) pH 6 and sandy loam OC 0.7% pH 6.6	48–92 % recovered in leachate as Nicosulfuron	Very mobile	Not reported
		Sandy clay loam OC 0.9% pH 5.9 Sandy clay loam OC 6.9% pH 5.8 Loam OC 1.3% pH 6.8 Loam OC 2.7% pH 6.0	68–82 % recovered as nicosulfuron in soils with OC 2.7% and 6.9% and 15–17% recovered as nicosulfuron in OC 0.9% and 1.3%	Very mobile	ASDM and ADMP 23% in soil and 17–23% in leachate.

Study Type	Test Material	Study Conditions	Value or Endpoint	Interpretation	Major Transformation Products
		Silt loam OC 1.4% pH 6.1	50% recovered in leachate as Nicosulfuron	Very mobile	Not reported
Soil lysimeter leaching	Nicosulfuron	Three year study. Pyrimidine-2-^{14}C Surface layer loamy sand 0–30 cm OC 1.1% pH 6.1 Lowest layer sand 90–120 cm OC 0% pH 7.3	3% leached through lysimeter Residue conc. in lower 60 cm of soil column 0.5% Total recovered AR 35–38%	Not significantly mobile below 0.5 m	CO_2
		Three year study. Pyridine-2-^{14}C Surface layer loamy sand 0–30 cm OC 1.1% pH 6.1 Lowest layer sand 90–120 cm OC 0% pH 7.3	2.4% leached through lysimeter. Total recoverable AR 83–84%.	Not significantly mobile below 0.5 m	CO_2
Field Studies					
Field dissipation	Nicosulfuron	2 Canadian and 1 US Site		DT_{50} DT_{90} Max Depth	DT_{50}
		Saskatchewan - loam - clay loam	SK loam - clay loam	34.7 d 115 d	SK site IN-V9367 473 d
		Manitoba - clay loam	MB clay loam	92.1 d 306 d	MN site IN-V9367 10 d
		Illinois - silty clay loam, clay loam, silty loam	Illinois silty clay loam, clay loam, silty loam	24–27 d 209–212 d 76 cm	Illinois site IN-V9367 Illinois site IN-J2090
		Supplemental Data Not Representative of Canadian Conditions:			
		California - sandy loam	California sandy loam	36–45 d 238–258 d 76 cm	California site IN-V9367,
		Germany - sand	Germany sand	8 d 87 d 30 cm	IN-37740
		Germany - silty clay loam	Germany silty clay loam	42 d 140 d 10 cm	Germany ADMP, ASDM
		France - loam	France loam	14 d 46 d 20 cm	France ADMP, ASDM
		France - clay loam	France clay loam	5 d 10 cm	

Table 2 Environmental Toxicity of Nicosulfuron and Its Transformation Products

Organism	Study Type	Species	Test Material	Endpoint	Value (effect)	Effect of Concern
Terrestrial Species						
Invertebrate	Acute oral	Honeybee (*Apis mellifera*)	Nicosulfuron active	48 h LD_{50}	>20 µg a.i./bee	Mortality
		Honeybee (*Apis mellifera*)	End-use product	48 h LD_{50}	>131 µg/bee	Mortality
		Honeybee (*Apis mellifera*)	Nicosulfuron 75% + surfactant IN KG 691	48 h LD_{50}	>100 µg/bee	Mortality
	Acute contact	Honeybee (*Apis mellifera*)	Nicosulfuron active	48 h LD_{50}	23 µg a.i./bee	Mortality
	Acute contact	Earthworm (*Eisenia foetida*)	Nicosulfuron active	14 d LC_{50}	1000 mg a.i./kg dr soil	Mortality
		Earthworm (*Eisenia foetida*)	Nicosulfuron 75% + surfactant DPX GFJ 47	7 and 14 d NOEC	500 mg /kg soil	Mortality
		Earthworm (*Eisenia foetida*)	Nicosulfuron 75% + surfactant IN KG691	14 d NOEC	1000 mg/kg soil	Mortality
		Earthworm (*Eisenia foetida*)	ASDM	14 d NOEC	1000 mg/kg dry soil	Mortality
		Earthworm (*Eisenia foetida*)	AUSN, HMUD, UCSN	7 d NOEC	1250 mg/kg dry soil	Mortality

Organism	Study Type	Species	Test Material	Endpoint	Value (effect)	Effect of Concern
		Earthworm (*Eisenia foetida*)	End-use product	14 d NOEC	1000 mg/kg soil	Mortality
		Honey bee (*Apis mellifera*)	Nicosulfuron active	48 h LD_{50}	>76 µg a.i./bee	Mortality
		Honeybee (*Apis mellifera*)	Nicosulfuron 75% + sufactant IN KG691	96-h LD_{50}	23 µg/bee	Mortality
		Honeybee (*Apis mellifera*)	Nicosulfuron 75% + sufactant IN KG691	48 h LD_{50}	37 µg/bee	Mortality
		Predatory mite (*Typhlodromus pyri*)	Nicosulfuron 75% + sufactant IN KG691	7 d LD_{50}	65 g/ha	Mortality
		Parasitic wasp (*Aphidius rhopalosiphi*)	Nicosulfuron 75% + sufactant IN KG691	48 h LD_{50}	298 g/ha	Mortality
Birds	Acute oral	Bobwhite quail (*Colinus virginianus*)	Nicosulfuron active	LD_{50}	>2000 mg a.i./kg bw	Mortality
		Mallard duck (*Anas platyrhynchos*)		LD_{50}	>2000 mg a.i./kg bw	Mortality
	Dietary	Bobwhite quail (*Colinus virginianus*)	Nicosulfuron active	LD_{50}	>5000 mg a.i./kg diet	Mortality
		Mallard duck (*Anas platyrhynchos*)		LD_{50}	>5000 mg a.i./kg diet	Mortality

Organism	Study Type	Species	Test Material	Endpoint	Value (effect)	Effect of Concern
	Reproduction	Japanese Quail (*Coturnix Japonica*)	Nicosulfuron active	NOEC	1000 mg a.i./kg diet	Reproduction
		Bobwhite quail (*Colinus virginianus*)		NOEC	1250 mg a.i./kg diet	Reproduction
		Mallard duck (*Anas platyrhynchos*)		NOEC	1250 mg a.i./kg diet	Reproduction
Mammals	Acute oral	Rat	Nicosulfuron active	LD_{50}	>5000 mg a.i./kg bw	Mortality
		Mouse	Nicosulfuron active	LD_{50}	>2600 mg a.i./kg bw	Mortality
	Dietary	Rat	Nicosulfuron active	13 w NOEC	50 000 mg a.i./kg diet	Growth
		Mouse	Nicosulfuron active	6 w NOEC	50 000 mg a.i./kg diet	Growth
	Reproduction	Rat - females	Nicosulfuron active	NOEC (2-generation)	500 mg a.i./kg diet	Reproduction
		Rat - males	Nicosulfuron active	NOEC (2-generation)	50 000 mg a.i./kg diet	Reproduction
Plants	Seedling emergence	Canola Oilseed *Brassica esculentum*	Nicosulfuron active	EC_{25} NOEL	0.504 g a.i./ha 0.273 g a.i./ha	Height
	Seedling emergence	19 plant species	Nicosulfuron active	EC_{25} NOEL	0.504–>125 g a.i./ha 0.273–>70 g a.i./ha	Height and % emergence

Organism	Study Type	Species	Test Material	Endpoint	Value (effect)	Effect of Concern
	Vegetative vigour	Nicosulfuron active *Brassica napus*	Nicosulfuron active	EC_{25} NOEL	0.838 g a.i./ha <0.0586 g a.i./ha	Dry Wt
	Vegetative vigour	18 plant species	Nicosulfuron active	EC_{25} NOEL	0.838–>62 g a.i./ha <0.0586–60 g a.i./ha	Dry Wt or Fresh Wt
Freshwater Organisms						
Invertebrates	Acute	*Daphnia magna*	Nicosulfuron active	48-h EC_{50} 48-h NOEC	90 mg a.i./L 32.4 mg a.i./L	Immobility
		Daphnia magna	75% active + DPX-GFJ47 surfactant	48-h LC_{50}	1.29 mg a.i./L	
		Daphnia magna	75% active + IN-KG691 surfactant	48-h LC_{50}	9.8 mg/L	
		Chironomus riparius	Nicosulfuron active	48-h LC_{50} 48-h NOEC	>200 mg a.i./L 200 mg a.i./L	
		Daphnia magna	AUSN, HMUD, UCSN	48-h LC_{50} 48-h NOEC	>100 mg/L 100 mg/L	
		Daphnia magna	ASDM	48-h LC_{50}	954 mg/L	
	Chronic	*Daphnia magna*	Nicosulfuron active	21-d LC_{50} 21-d NOEC	>710 mg a.i./L 43 mg a.i./L	Immobility
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	Nicosulfuron active	96-h LC_{50}	0.375 mg a.i./L	Mortality
			Nicosulfuron active	96-h LC_{50} 96-h NOEC	65.7 mg a.i./L 19.4 mg a.i./L	
			75% active + DPX-GFJ47 surfactant	96-h LC_{50}	3.5 mgi/L	

Organism	Study Type	Species	Test Material	Endpoint	Value (effect)	Effect of Concern
			75% active + IN KG 691 surfactant	96-h LC_{50}	8.49 mg/L	
			AUSN, HMUD, UCSN	96-h LC_{50} 96-h NOEC	>100 mg/L 100 mg/L	
			ASDM	96-h LC_{50} 96-h NOEC	>996 mg/L 251 mg/L	
			End-use product	96-h LC_{50}	55.6 mg/L	
		Bluegill *(Leopomis machrochirus)*	Nicosulfuron active	96-h LC_{50} 96-h NOEC	>100 mg a.i./L 100 mg a.i./L	
		Rainbow trout (*Oncorhynchus mykiss*)	End-use product	96-h LC_{50} 96-h NOEC	55.6–100 mg/L 17.1 mg/L	
		Bluegill *(Leopomis machrochirus)*	End-use product	96-h LC_{50} 96-h NOEC	124.6 mg/L 34.3 mg/L	
		Carp	End-use product	96-h LC_{50}	100 mg a.i./L	
	Chronic (Early Life Stage)	Rainbow trout (*Oncorhynchus mykiss*)	Nicosulfuron active	90-d LC_{50} 90-d NOEC	>99 mg a.i./L 24 mg a.i./L	Reproduction Mortality eggs and fry
Algae	Acute	Green alga (*Selenastrum capricornutum*)	Nicosulfuron active	72-h EC_{50} 72-h NOEC	>6.4 mg a.i./L >6.4 mg a.i./L	Cell count
			Nicosulfuron active	72-h EC_{50} 72-h NOEC	3.32 mg a.i./L 0.561 mg a.i./L	Cell count
			ASDM	72-h EC_{50} 72-h NOEC	54.0 mg/L 10.2 mg/L	Not reported

Organism	Study Type	Species	Test Material	Endpoint	Value (effect)	Effect of Concern
		Blue green alga (*Anabaena flos-aquae*)	Nicosulfuron active	96-h EC_{50} 96-h NOEC	11.63 mg a.i./L 4.69 mg a.i./L	Cell count
			Nicosulfuron active	96-h EC_{50} 96-h NOEC	28.35 mg a.i./L 22.5 mg a.i./L	Growth curve
			Nicosulfuron active	72-h EC_{50} 72-h NOEC	7.8 - 8.4 mg a.i./L 3.2 mg a.i./L	Not reported
			75% active + DPX-GFJ47 surfactant	96-h EC_{50} 96-h NOEC	14.77 mg/L <4.68 mg/L	Cell count
		Alga (*Scenedesmus subspicatus*)	Nicosulfuron active	96-h EC_{50} 96-h NOEC	227 mg a.i./L 100 mg a.i./L	Not reported
			End-use product	72-h EC_{50} 72-h NOEC	>100 mg/L 100 mg/L	Not reported
			End-use product	72-h EC_{50} 72-h NOEC	3.50 mg/L 0.45 mg/L	Not reported
			AUSN	72-h EC_{50} 72-h NOEC	>100 mg/L 100 mg/L	Not reported
			HMUD	72-h EC_{50} 72-h NOEC	>100 mg/L 45.5 mg/L	Not reported
			UCSN	72-h EC_{50} 72-h NOEC	>100 mg/L 6.25 mg/L	Not reported
Vascular Plants	Acute	Duck weed (*Lemna gibba*)	Nicosulfuron active	7-d EC_{50} 7-d NOEC	0.028 mg a.i./L 0.035 mg a.i./L	Mortality Frond count
			75% active + IN KG691 surfactant	14-d EC_{50} 14-d NOEC	2.41 µg/L 0.751 µg/L	Frond count Frond count
			75% active + DPX-CFJ47 surfactant	14-d EC_{50} 14-d NOEC	2.86 µg/L 0.561 µg/L	Biomass Biomass

Organism	Study Type	Species	Test Material	Endpoint	Value (effect)	Effect of Concern
			ASDM, AUSN, USCN	7-d EC_{50} 7-d NOEC	>100 mg/L 100 mg/L	Not reported
			End-use product	7-d EC_{50} 7-d NOEC	0.06 µg/L 0.0233 µg/L	Frond count

Table 3 Summary of Screening Level Risk Assessment of Nicosulfuron and Transformation Products to Terrestrial Organisms

Organism	Exposure	Test Material	Endpoint Reported	Use Rate (g a.i./ha)	EEC	RQ*
Invertebrates						
Earthworm	Acute	Active	NOEC 1000 mg a.i./kg soil	12.5	5.6×10^{-3} mg a.i./kg soil	5.6×10^{-6}
				25	1.1×10^{-2} mg a.i./kg soil	1.1×10^{-5}
		75% active+ DPX-GFJ47	NOEC 500 mg a.i./kg soil	12.5	5.6×10^{-3} mg/kg soil	1.1×10^{-5}
				25	1.1×10^{-2} mg/kg soil	2.2×10^{-5}
		ASDM	NOEC 1000 mg a.i./kg soil	12.5	1.3×10^{-3} mg a.i./kg soil	1.3×10^{-6}
				25	2.6×10^{-3} mg a.i./kg soil	2.6×10^{-6}
Honeybee	Acute contact	75% active + IN-KG691	NOEC 2.3 µg a.i./bee (2576 g a.i./ha)	12.5	12.5 g a.i./ha	4.8×10^{-3}
				25	25.0g a.i./ha	9.7×10^{-3}
Birds						
Mallard	Dietary	Active	NOEC 5000 mg a.i./kg diet	12.5	0.42 mg a.i./kg diet	8.4×10^{-4}
				25	0.85 mg a.i./kg diet	1.7×10^{-3}
Bobwhite quail	Dietary	Active	NOEC 5000 mg a.i./kg diet	12.5	2.19 mg a.i./kg diet	4.4×10^{-3}
				25	4.38 mg a.i./kg diet	8.8×10^{-3}
Field sparrow	Dietary	Active	NOEC 3031 mg a.i./kg diet	12.5	1.47 mg a.i./kg diet	4.8×10^{-3}
				25	2.93 mg a.i./kg diet	9.7×10^{-3}
Japanese quail	Reproduction	Active	NOEC 1000 mg a.i./kg diet	12.5	2.19 mg a.i./kg diet	2.2×10^{-3}
				25	4.38 mg a.i./kg diet	4.4×10^{-3}

Organism	Exposure	Test Material	Endpoint Reported	Use Rate (g a.i./ha)	EEC	RQ*
Mammals						
Rat	Dietary	Active	NOAEL 5000 mg a.i./kg diet	12.5	6.31 mg a.i./kg diet	1.3×10^{-3}
				25	12.61 mg a.i./kg diet	2.5×10^{-3}
	Reproduction	Active	NOAEL 1263 mg a.i./kg diet	12.5	6.31 mg a.i./kg diet	8.6×10^{-4}
				25	12.61 mg a.i./kg diet	1.7×10^{-3}
Plants						
Plants	Seedling emergence (canola)	Active	EC_{25} 0.504 g a.i./ha	12.5	12.5 g a.i./ha	**24.8**
				25	25.0 g a.i./ha	**49.6**
	Vegetative vigour (canola)	Active	EC_{25} 0.838 g a.i./ha	12.5	12.5 g a.i./ha	**14.9**
				25	25.0 g a.i./ha	**29.8**

* Risk quotient values that are in bold font exceed the level of concern

Table 4 Refined Risk Assessment of Nicosulfuron to Terrestrial Plants

Organism	Exposure	EC_{25}	Use Rate (g a.i./ha)	% application rate to reach EC_{25} [1] (i.e. RQ = 1)	Drift EEC [2]	RQ [3]
Plants	Seedling emergence (canola)	0.504 g a.i./ha	12.5	4	0.75 g a.i./ha	**1.5**
			25	2	1.5 g a.i./ha	**3**
	Vegetative vigour (canola)	0.838 g a.i./ha	12.5	6.7	0.75 g a.i./ha	0.9
			25	3.3	1.5 g a.i./ha	**1.8**

1 % of application rate to reach RQ of 1 = (EC_{25}/Use Rate) × 100

2 Drift EEC = 6/100 × Use Rate. Based on drift of 6% for a medium droplet size (American Society of Agricultural Engineers).

3 RQ = Drift EEC/EC_{25}

Table 5 Summary of Screening Level Risk Assessment of Nicosulfuron and Transformation Products to Aquatic Organisms

Organism	Exposure	Test Material	Species	Endpoint Reported	Endpoint for RA*	Use Rate (g a.i./ha)	EEC** (mg a.i./L)	RQ
Freshwater Species								
Invertebrate	Acute	Active	*Daphnia magna*	LC_{50} 90 mg a.i./L	45 mg a.i./L	12.5	1.56×10^{-3}	3.5×10^{-5}
						25	3.13×10^{-3}	7.0×10^{-5}
	Acute	75% active+ DPX-GFJ47	*Daphnia magna*	LC_{50} 1.29 mg/L	0.645 mg/L	12.5	1.56×10^{-3}	2.4×10^{-3}
						25	3.13×10^{-3}	4.8×10^{-3}
	Acute	Active	Chironomid *C. Riparius*	LC_{50} 200 mg a.i./L	100 mg a.i./L	12.5	1.56×10^{-3}	1.6×10^{-5}
						25	3.13×10^{-3}	3.1×10^{-5}
	Acute	HMUD	*Daphnia magna*	LC_{50} 100 mg/L	50 mg/L	12.5	2.96×10^{-4}	5.9×10^{-6}
						25	5.95×10^{-4}	1.2×10^{-5}
	Chronic	Active	*Daphnia magna*	NOEC 43 mg a.i./L	43 mg a.i./L	12.5	1.56×10^{-3}	3.6×10^{-5}
						25	3.13×10^{-3}	7.3×10^{-5}
Fish	Acute	Active	Rainbow trout	LC_{50} 0.375 mg a.i./L	0.0375 mg a.i./L	12.5	1.56×10^{-3}	4.0×10^{-2}
						25	3.13×10^{-3}	8.0×10^{-2}
	Acute	75% active+ DPX-GFJ47	Rainbow trout	LC_{50} 3.5 mg/L	0.35 mg/L	12.5	1.56×10^{-3}	4.5×10^{-3}
						25	3.13×10^{-3}	8.9×10^{-3}
	Acute	End-use product	Rainbow trout	LC_{50} 55.6 mg/L	5.56 mg/L	12.5	1.56×10^{-3}	3.0×10^{-4}
						25	3.13×10^{-3}	6.0×10^{-4}

Organism	Exposure	Test Material	Species	Endpoint Reported	Endpoint for RA*	Use Rate (g a.i./ha)	EEC** (mg a.i./L)	RQ
	Acute	End-use Product	Carp	LC_{50} 47.3 mg/L	4.73 mg/L	12.5	1.56×10^{-3}	3.0×10^{-4}
						25	3.13×10^{-3}	7.0×10^{-4}
	Acute	HMUD	Zebra fish	LC_{50}100 mg/L	10.0 mg/L	12.5	2.96×10^{-4}	3.0×10^{-5}
						25	5.95×10^{-4}	6.0×10^{-5}
	Chronic	Active	Rainbow trout (Early Life Cycle)	NOEC 24 mg a.i./L	24 mg a.i./L	12.5	1.56×10^{-3}	6.5×10^{-5}
						25	3.13×10^{-3}	1.3×10^{-4}
Plant	Acute	Active	Duckweed *Lemna gibba*	EC_{50} 0.28 mg a.i./L	0.014 mg a.i./L	12.5	1.56×10^{-3}	1.1×10^{-1}
						25	3.13×10^{-3}	2.2×10^{-1}
		75% active + IN KG691	Duckweed *Lemna gibba*	EC_{50} 2.41 mg/L	1.21 mg/L	12.5	1.56×10^{-3}	1.3×10^{-3}
						25	3.13×10^{-3}	2.6×10^{-3}
		End-use product	Duckweed *Lemna gibba*	EC_{50} 0.06 mg/L	0.03 mg/L	12.5	1.56×10^{-3}	5.2×10^{-2}
						25	3.13×10^{-3}	1.0×10^{-1}
	Acute	HMUD	Alga *S. Capricornutum*	EC_{50} 100 mg/L	50 mg/L	12.5	2.96×10^{-4}	5.9×10^{-6}
						25	5.95×10^{-4}	1.2×10^{-5}

Organism	Exposure	Test Material	Species	Endpoint Reported	Endpoint for RA*	Use Rate (g a.i./ha)	EEC** (mg a.i./L)	RQ
Amphibian	Acute	Active	Rainbow trout (surrogate)	LC_{50} 0.375 mg a.i./L	0.0375 mg a.i./L	12.5	8.33×10^{-3}	2.2×10^{-1}
						25	1.67×10^{-2}	4.4×10^{-1}
	Acute	75% active+ DPX-GFJ47	Rainbow trout (surrogate)	LC_{50} 3.5 mg/L	0.35 mg/L	12.5	8.33×10^{-3}	2.4×10^{-2}
						25	1.67×10^{-2}	4.8×10^{-2}
	Acute	End-use product	Rainbow trout (surrogate)	LC_{50} 55.6 mg/L	5.56 mg/L	12.5	8.33×10^{-3}	1.5×10^{-3}
						25	1.67×10^{-2}	2.9×10^{-3}
	Acute	HMUD	Zebra fish (surrogate)	LC_{50}100 mg/L	10.0 mg/L	12.5	1.58×10^{-3}	1.6×10^{-4}
						25	3.17×10^{-3}	3.1×10^{-4}
	Chronic	Active	Fish Early Life Cycle (surrogate)	NOEC 24 mg a.i./L	24 mg a.i./L	12.5	8.33×10^{-3}	3.5×10^{-4}
						25	1.67×10^{-2}	6.9×10^{-4}

* Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.

** EEC based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic organisms.

Appendix XI Label Amendments for Commercial Class Products Containing Nicosulfuron

Canadian commercial end-use product labels must be amended to include the following statements to further protect workers and the environment.

FOR ALL FORMULATIONS:

Add to **DIRECTIONS FOR USE:**

- Do not re-enter treated fields until 12 hours after application.
- Apply only when the potential for drift to areas of human habitation or areas of human activity (houses, cottages, schools and recreational areas) is minimal. Take into consideration wind speed, wind direction, temperature, application equipment and sprayer settings.

General Restrictions:

- DO NOT apply this product to any body of water.
- DO NOT contaminate irrigation/drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

Spray application:

- DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply with spray droplets smaller than the ASAE medium classification.
- DO NOT apply by air.

Buffer zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer, inter-row hooded sprayer, spot treatment, soil drench, and soil incorporation.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, pastures, rangelands, and shrublands).

Application Rate (g a.i./ha)	Buffer zone (metres) required for the protection of terrestrial habitat
25	2
12.5	1

For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy, the labelled buffer zone can be reduced by 30%.

When a tank mixture is used, consult the labels of the tank-mix partners and use the largest (most restrictive) buffer zone recommended for any of the products.

Add to **ENVIRONMENTAL HAZARDS:**

TOXIC to terrestrial plants and aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE.

To reduce runoff from treated areas into aquatic habitats, avoid areas with a moderate to steep slope, compacted soil or clay.

Avoid application of this product when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

Add to **PRECAUTIONS:**

- Wear long-sleeved shirt, long pants, socks, and chemical-resistant gloves and footwear during mixing, loading, application, clean-up and repair. Chemical-resistant gloves are not required while operating groundboom sprayers.

FOR WETTABLE GRANULE FORMULATIONS:

Add to **DIRECTIONS FOR USE:**

- Nicosulfuron is formulated as a wettable granule sealed within a water-soluble package (WSP). Drop intact WSP directly into spray tank. The WSP and pesticide will dissolve readily in water.
- Do not allow the WSP to become wet prior to use. Do not handle individual WSP with wet hands or wet gloves as this may cause breakage. Do not remove WSP from over-wrap container except for immediate use.
- Do not open WSP or attempt to remove the contents from them. The contents are not designed to be re-measured or subdivided.
- Do not use opened or punctured WSP.
- If broken WSP is found when the over-wrap bag is opened, avoid contact with, and inhalation of the product. Handle with chemical-resistant gloves and dispose of broken WSP according to the DISPOSAL section.

Appendix XII Supplemental Maximum Residue Limit Information– International Situation and Trade Implications

Nicosulfuron residues resulting from Canadian label uses on blueberry are covered by B.15.002(1) of the Food and Drug Regulations, while general regulation B.15.002(1) applies to all foods where a specific MRL has not been established for corn. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2003-01, *Revocation of the 0.1 ppm General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*.

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data.

Table 1 Comparison between MRLs in Canada and in Other Jurisdictions

Commodity	MRL or Tolerance (ppm)		
	Canada[1]	United States[2]	Codex[3]
Blueberry	0.05	None	None
Corn	0.1	0.1	None

Notes

1 By virtue of subsection B.15.002(1) of the Food and Drug Regulations, the MRL of foods for which MRLs have not specifically been established is 0.1 ppm.

2 As per Title 40 Part 180.454 of the United States Code of Federal Regulations..
See also www.access.gpo.gov/nara/cfr/waisidx_01/40cfr180_01.html

3 Codex is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.
See also www.mrldatabase.com

Table 2 Residue Definition in Canada and Other Jurisdictions

Jurisdiction	Residue Definition
Canada	2[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino] sulfonyl]-*N,N*-dimethyl-3-pyridinecarboxamide
United States	[3-pyridinecarboxamide, 2-((((4,6-dimethoxypyrimidin-2-yl)aminocarbonyl)aminosulfonyl))-N,N-dimethyl]
Codex (JMPR)	None